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EXPERIMENTAL METHODS FOR DETECTION OF CHANGES OF BLOOD SUPPLY TO THE HEART

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THE introduction of surgical procedures to produce an auxiliary blood flow to the myocardium for coronary artery disease has posed new problems. O'Shaughnessy's[1] omentopexy was designed to bring blood to the ischemic myocardium from the mesenteric circulation by transplanting the omentum to the surface of the myocardium. Beck's[2-6] pectoral transplant and intrapericardial scarification combined with instillation of talc or asbestos was calculated not only to bring auxiliary blood supply via the pectoralis muscle but also to produce vasodilatation of the coronary circulation and thus to increase its natural collateral circulation.[7-8] Thompson's[9, 10] cardiopericardiopexy utilized asbestos particles inserted into the pericardium to increase natural collateral circulation. Beck's[11, 12] operation of transplanting a systemic artery into the coronary sinus was designed to bring systemic blood flow as an auxiliary source of blood to the myocardium via retrograde flow through the coronary venous system. Vineberg[13] implanted the internal mammary artery into the myocardium thus producing auxiliary blood flow directly to the muscular channels of the myocardium. Ligation of the coronary sinus was designed to increase the arteriovenous collateral coronary circulation.[14] Beck's newest two-stage operation appears to be most promising. In the first stage a 3 to 4 mm. sized connection between the ascending aorta and the coronary sinus is made with a vein graft. A few weeks later at the second operation the coronary sinus is stenosed with a

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Nylon ligature. This operation brings arterial systemic blood with a high-pressure gradient into the venous system of the myocardium.[15] It would appear that arteriovenous anastomoses would be a necessary pathway for such retrograde flow to effectively reach the myocardial capillary system.

Thus the surgical procedures so far have been concerned with:

1. Irritating the myocardium so as to produce vasodilatation and vascular intrapericardial adhesions.
2. Bringing new systemic arterial blood supply to the surface of the myocardium with pedicled omentum, pectoralis muscle or lung.
3. Bringing arterial blood supply directly to the myocardium or coronary sinus.

The chief problem concerning these surgical procedures is how to evaluate their effectiveness as auxiliary collateral coronary circulations. To do this, methods for detection of changes in the myocardial blood supply are necessary since ischemia is the chief process being corrected by the surgically induced collateral circulation.

All these surgical procedures have been designed to increase the normal physiologic collateral circulation of the myocardium. The tests of benefit from the newly acquired circulation have almost exclusively been worked out on dogs.[15] In dogs, surgically induced auxillary vascular supplies to the myocardium have been shown to exist by anatomic studies.[16, 17] Physiologically, bleeding experiments from the distal cut end of the coronary arteries after ligation of the proximal end, and survival experiments following coronary ligation, have indicated the functional state and effectiveness of the surgically induced collateral coronary circulation.[15] It is hoped that such surgically induced additions to the normal myocardial collateral circulation may protect against coronary insufficiency and further ischemia associated with effort, blood pressure changes, and additional infarcts.

To better understand the problem of evaluating the effectiveness of surgically induced, auxiliary collateral blood supply to the coronary circulation we shall now review in brief some of the experimental observations made in this laboratory which show the nature of the collateral coronary circulation in normal and ischemic hearts of both dog and man:[18-21]

1. By the use of saline suspension of erythrocytes labeled with radioactive phosphorus, the existence of numerous anastomoses in the left ventricle and of a collateral circulation between the right and left ventricles was demonstrated in the normal post-mortem human heart.
2. By the use of measurable glass spheres ranging in diameter from 10 to 400 micra the largest intercoronary arterial anastomosis in the normal human heart was found to allow the passage of spheres ranging from 70 to 180 micra. These findings indicate that such intercoronary arterial anastomoses are of arteriolar dimensions in the normal heart.

3. Arteriovenous coronary anastomoses were demonstrated by recovery of glass spheres 70 to 170 micra in diameter from the coronary sinus after their injection into the right or left coronary arteries.
4. The diameters of the anastomotic channels between the coronary arteries and either of the ventricular cavities range from 70 to 220 micra. These channels represent one or all of the following vessels: arterioluminal, arteriosinusoidal, and Thebesian veins.
5. By intravenous injection of labeled erythrocytes into moribund patients with normal and ischemic myocardiums, the presence of a functioning collateral circulation to all parts of the myocardium was demonstrated including the infarcted areas.
6. From the observations with intravascularly injected erythrocytes it was concluded that the collateral circulation to the myocardium of the dog, which had been rendered ischemic by ligation of the anterior descending coronary artery, supplies all parts of the ischemic region; furthermore this collateral supply of blood circulates actively throughout the ischemic area, but the pericardial side of ischemic myocardium of the left ventricle is better nourished by the collateral circulation than the endocardial side.
7. In shock not only is the general systemic blood pressure lowered but also the coronary blood pressure. Under conditions of shock the collateral circulation to an area of the myocardium, made ischemic by ligation of the anterior descending coronary artery, has little or no function since the blood pressure is too low for pumping blood efficiently through the collateral circulation.
8. The reverse was also shown to be true. If the blood pressure was raised by transfusion of heparinized blood, the collateral circulation to an ischemic area was restored.

The preceding discussion has described changes in the collateral coronary circulation that can be found in all normal dogs' beating hearts. Just as ingestion of carbohydrate elicits an increased output of insulin, the production of myocardial ischemia calls forth an increase of collateral coronary circulation. The problem is how best to detect and evaluate that additional collateral blood supply induced by experimental surgical procedures. For obvious reasons, it would appear desirable to have visual tests which may be performed upon the dog's beating heart rather than to depend upon findings in dead hearts. Likewise, it is desirable to have tests which have already had a base line of experimental detection of normal coronary collateral circulation. It is the purpose of this paper to present three visual methods for detecting changes of blood supply to the dog's beating heart. These tests are: (1) fluorescein, (2) contractility, and (3) electrical activity.*

*A colored motion picture was shown to illustrate the three tests.

FLUORESCEIN

Prinzmetal and associates[18-21] have shown previously that the coronary circulation can be visually demonstrated in the dog's beating heart by slow motion pictures (50 to 100 frames per second), photographed under near ultraviolet light to allow the intravenously injected fluorescein to become visible within the coronary circulation. The following observations are pertinent to the use of fluorescein as a test of benefit from the additional collateral circulation which might be supplied to the myocardium by the particular surgical procedure:

1. In animals with normal blood pressure, fluorescein appeared in the coronary arteries rapidly, 4 to 7 seconds, and in the next few seconds the entire heart became intensely fluorescent.
2. If the dye were injected directly into only one artery, the anterior descending artery of a dog's beating heart, the dye could be visualized in the coronary circulation of an area many times greater than that normally supplied by the anterior descending coronary artery.
3. It was visually demonstrated that the coronaries were not end arteries and that there was physiologic coronary collateral circulation in the normal dog's myocardium detectable by the fluorescein method.
4. In shock, induced by hemorrhage, diminution of the coronary blood flow could be demonstrated since the appearance time and intensity were delayed but all the coronary circulation eventually visualized.
5. When fluorescein was injected into the femoral vein after the mid-anterior descending artery was ligated in dogs with normal blood pressure the fluorescein rapidly filled the ischemic region from contiguous areas.
6. The ischemic regions generally became intensely fluorescent 1 to 2 seconds after the control regions.
7. If the blood pressure were lowered to shock levels (20 to 50 mm. of Hg mean pressure) the appearance time in the infarcted ischemic areas was markedly prolonged or even absent. The blood pressure was too low to pump the fluorescein through the collaterals and so the infarcts did not visualize with fluorescein.
8. The reverse was also shown to be true if a dog (in shock with coronary artery ligated) had his blood pressure restored with transfusion of heparinized blood, the fluorescein test showed the ischemic area to fill from contiguous areas through the normal collateral circulation.

By the fluorescein test the ischemia of shock and of experimental coronary infarction was readily detected. From the observations above listed it can be concluded that there is an always ready, normal, natural collateral coronary circulation which, however, has limited effect upon myocardial ischemia. Probably small arterially occluded muscle masses are rendered relatively normal and completely protected. But larger ischemic muscle masses may re-

sult in central necrosis of the myocardium when the collateral circulation is not adequate. Furthermore persistence of nonfilling, central cyanosis of the infarcted area during fluorescein test indicates that no collateral circulation is effective for this area. The normal predicted response for the physiologic collateral circulation after ligation of the anterior descending artery of a dog's beating heart would be only a second or two delay of the fluorescein into the ischemic area. It is suggested that additional collateral blood supplied by experimental surgical procedures ought to be detected by this method. If the new blood supply were efficient it should allow fluorescein to fill areas made ischemic by coronary ligation with but slight delay in appearance time since the new blood flow would not be interrupted by the coronary ligation. If the additional blood flow from the operative procedure were 100 per cent efficient, the predicted visualization with fluorescein would approach that of the normal contiguous areas and the muscle mass supplied by the ligated coronary artery should not appear ischemic. For these reasons we feel that the fluorescein can be offered as a test of the benefit which might be derived from experimental surgically induced auxiliary collateral coronary circulation.*

CONTRACTILITY

Ischemic myocardium ceases to contract within 3 to 4 seconds after the anterior descending coronary artery is ligated.[22, 23] In a dog's beating heart this cinematographic phenomenon of noncontractility of the muscle mass supplied by the ligated anterior descending artery is called "ballooning." Sometimes this phenomenon occurs only in late systole, but in other instances the ischemic region balloons during the entire systolic phase. Ballooning after ligation of small arteries may come and go, or even not occur at all, but larger ischemic areas balloon more consistently. After inducing hemorrhagic shock in dogs with coronary infarcts, the following significant changes occurred as a result of the low blood pressure in the slow motion colored movies:

1. The ballooning became much more extensive in area and degree.
2. Cyanosis of the ischemic area became marked.
3. If ballooning had disappeared spontaneously, it reappeared and became more marked.
4. If there was only late systolic "ballooning" and not full systolic "ballooning," it now occupied the full phase of systole.

The reversibility of "ballooning" could be induced by transfusing with heparinized blood and restoring the blood pressure from shock levels to normal. Such transfusions resulted in restoring the noncontractile "ballooning" to visibly normal contractions in the cinematographic observations. Not only did the "ballooning" cease or become less intense but the cyanosis also diminished or disappeared as the blood pressure was restored to normal. The observation that the "ballooning" is associated with myocardial ischemia can also be substantiated by the fluorescein test which shows slow or absent filling in the "ballooning" areas.

*Colored photographs from the slow motion movie with fluorescein are published in the American Heart Journal, Vol. 35, page 18, May, 1948. See reference No. 19.

These experiments show that "ballooning" is associated with myocardial ischemia since it occurs after experimental production of ischemic infarcts. Furthermore the "ballooning" appears to vary with the effectiveness of the collateral coronary blood flow. Therefore "ballooning" should be suitable as a test of benefit for detecting the effectiveness of additional artificially supplied blood from surgical procedures. Efficient surgically produced collateral blood supplies should protect against the phenomenon of "ballooning" when myocardial ischemia is experimentally produced by ligation of the anterior descending coronary artery in the dog's beating heart. Less suitable and less efficient surgical procedures would probably not prevent the occurrence of "ballooning" after experimental coronary ligation. For these reasons we feel that "ballooning" can be offered as a test of benefit.

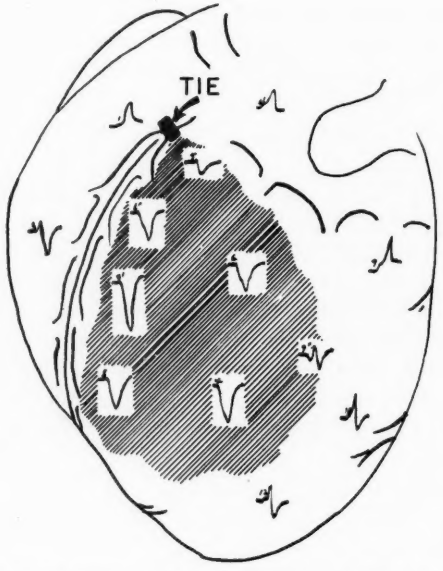

Fig. 1.—Diagram taken from data showing electrical activity in a dog's beating heart with a "through and through" infarct of two months' duration. Tie is on the anterior descending coronary artery. Shaded area is the grossly ischemic region. Within the shaded area the explored spots record a Q wave. At the edges where there is less ischemia QR waves are recorded in the left ventricle and over the normal left ventricle R and RS waves are recorded.

ELECTRICAL ACTIVITY

Since the electrical activity of the myocardial contraction is related to the efficiency of the coronary circulation, an electrocardiographic test of benefit induced by surgically made auxiliary collateral coronary circulation should be feasible. To study this problem experimentally, the anterior descending coronary artery in sixty dogs was ligated. These operations were performed through an intercostal approach with a 4-inch incision in the left fifth interspace. The dogs were prepared with morphine (.003 Gm. per kilogram) and atropine (.00004 Gm. per kilogram) in suitable doses and anesthesia was main-

tained with intravenous sodium pentothal. Continuous ventilation of the lungs was made through a semirigid intratracheal catheter and the portable Waters-Guedel anesthesia apparatus. One hundred per cent oxygen was the ventilating gas, administered by intermittent manual compression of the 3 liter rubber bag.* The wound was closed air tight with the lungs fully inflated in order to avoid leaving any appreciable pneumothorax. Postoperatively one or two intramuscular injections of penicillin-streptomycin mixture (400,000 units of the former and 1 Gm. of the latter) were administered daily for one or two days. Although practically all the ligations were performed at a relatively high level, the mortality was approximately 15 per cent from immediate ventricular fibrillation. Only one delayed mortality occurred from empyema.

Fig. 2.—Enlarged still photograph from a high-speed colored movie picture frame. In this experiment the exploring electrode has a knob and is to the left and it records the lower tracing. Being over a normal area it records an upright positive R wave. The tiny silver electrode in the left ventricular cavity is just to the right and it records on the upper tracing a cavitary Q wave.

After various intervals, up to six months, the surviving animals were then prepared for electrocardiographic studies. The chest was opened bilaterally, and the sternum was partially removed, together with suitable portions of the ribs. Anesthesia was morphine and intravenous urethane, and the lungs were ventilated continuously with 100 per cent oxygen with a suitable artificial pump and an intratracheal catheter. Although in some instances the pericardium was not opened, most of the electrocardiographic tracings were made on the exposed myocardium after suturing the opened pericardium to the chest wall. Electrical activity was recorded with a double channel high-speed pen writing Brush recorder at 125 mm. per second. The exploring electrode recorded the electrical activity directly from the surface of the myocardium of any desired spot.

*Anesthesia was administered by Dr. David Sobin and the operative assistant was Dr. I. Alfred Breckler.

Electrocardiographic recording was performed with the aid of a unipolar system using the Wilson central terminal. Routinely, as many as 40 or 50 chosen spots representative of both ventricles and the ischemic infarcted areas were explored (Fig. 1). A special silver-needle, insulated, reference electrode, made so as to record only from its tip, was plunged into the left ventricular cavity in

Fig. 3.—Same experiment as Fig. 2 of an electrocardiographic exploration of the surface of a dog's beating heart with a two-month-old "through and through" infarct. The exploring electrode is now over a fibrous area and it records on the lower tracing a Q wave almost the same as the cavitary Q wave recorded on the upper tracing.

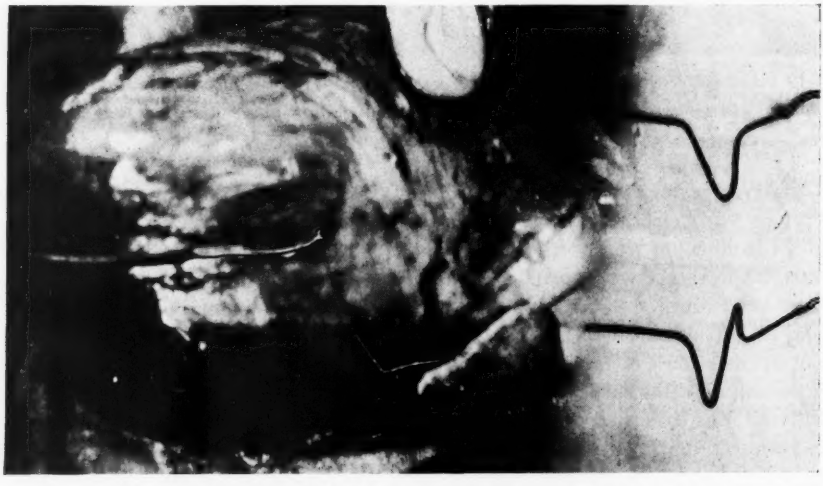

Fig. 4.—The exploring electrode is now moved over an area in the infarct with less fibrous tissue replacement and more contractile muscle mass and it records a QR wave in the lower tracing, while the reference electrode continues to record a cavitary Q wave.

order to record simultaneously the left ventricular cavity potential. Simultaneously, the dog's beating heart and the electrocardiographic tracings were photographed in color at high speed so that visible contractility and electrical activity appeared in the same frame when the movie was projected. Although pathologic studies were made of all hearts, and special studies were also carried out for purposes of determining the exact origin of the electrocardiographic tracings obtained, only the Q, R, and QR wave changes will be reported here.

In infarcts of one or two months' duration, the surface was whitish on the pericardial side. Often myocardial contractility was visibly diminished over these areas. Over the normal areas of the left ventricle, not expected to be supplied by the anterior descending artery, usually normal red in color, and with good contractility, a positive deflection of an R or RS wave was consistently recorded (Figs. 1, 2, and 5). Over the center of such infarcted whitish areas, or where no contractility in the whitish areas was present, a Q wave was recorded

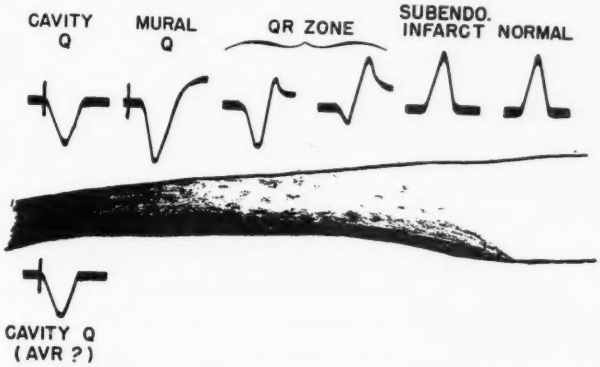

Fig. 5.—Diagrammatic representation of the type of electrocardiographic tracing obtained from the surface of the dog's beating heart correlated with the amount of infarction and its location. The completely shaded area represents "through and through" infarct and successively less involvement proceeding from left to right until only a subendocardial infarct and finally normal muscle is encountered. It can be seen as one proceeds from left to right, there is less Q and more R until the normal area is reached.

(Fig. 3). As the exploring electrode was moved toward the periphery of the infarct from its center, less ischemic areas were encountered where QR waves were recorded (Fig. 4). Over old infarcts with complete replacement of myocardium by fibrous tissue the exploring electrode recorded Q waves with the same configuration as the Q waves recorded by the cavity electrode (Fig. 3). The histologic examination of the infarcted areas confirmed the finding that the more fibrous tissue replacement in the myocardium, the more Q and less R wave was present (Fig. 5). In infarcts where the myocardium had not become ischemic "through and through," various quantities of muscle tissue may still be viable and contractile. In these areas of less ischemia, QR waves are often present (Figs. 1, 4, and 5).

It would appear that measurement of electrical activity of the dog's beating heart by the method described is suitable for detecting ischemic areas of infarct following ligation of the anterior descending coronary artery. This is so because

as one went from ischemic to normal myocardium there was less Q and more R or QR waves, and because there was a histopathologic correlation in the infarcts examined, so that the more fibrous tissue replacement the more Q wave, and the more contractile muscle the more R or QR wave (Fig. 5). It is hoped that when applied as a test of benefit for surgical procedures producing auxiliary blood supplies to the heart, this electrocardiographic method will be satisfactory. Thus in a dog's beating heart, previously prepared with an efficient auxiliary collateral blood supply, these Q waves of myocardial ischemia should not be recorded over the occluded muscle mass after ligation of the anterior descending coronary artery.

SUMMARY AND CONCLUSION

1. It was stated that most surgical procedures being used in the management of coronary artery disease are designed to increase the normal, natural collateral circulation of the myocardium. Such surgical procedures are in need of objective methods of evaluation in the dog's beating heart.

2. Fluorescein injected intravenously may be used to detect changes in blood supply to the myocardium in the dog's beating heart when photographed in color under near ultraviolet light at 50 to 100 frames per second.

3. In similar slow motion movies of the dog's beating heart, alterations in myocardial contractility can be visualized after ligation of the anterior descending coronary artery. This loss of contractility is associated with ischemia of the occluded muscle mass and results in the cinematographic visualization termed "ballooning."

4. Electrocardiographic tracings of experimental coronary infarcts taken directly from the surface of the dog's beating heart showed that the "through and through" ischemic areas could be detected by the Q waves reported over them. The more ischemic the myocardium, the more Q wave; the less ischemic the myocardium, the more R wave was recorded. In intermediate areas QR waves were recorded.

5. These three visual methods utilizing fluorescein, contractility, and electrical activity of the dog's beating heart are offered as tests of benefit from surgically induced auxiliary collateral coronary circulation.

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DISCUSSION

DR. OSLER ABBOTT, Atlanta.—I certainly feel that Dr. Goldman is to be congratulated in presenting us with another approach in regard to experimentation, which certainly has a tremendous potential. I would like to mention briefly some work which has been carried out by the Medical School at Emory University and the Georgia Institute of Technology. They have perfected a camera system which allows an excellent visualization of the human coronaries in action by intravenous diodrast angiocardiography. Some of you, I am sure, viewed this film at the meeting of the Southern Medical Association last fall. This has many applications in the study of the circulation of the lung before and after operative procedures for emphysema. The major benefits are three. One is research value, for by using 16 to 64 film exposures per second and then converting it to slow motion, we can study motions too fast for the human eye. It also allows study of bronchial motility and esophageal motility too rapid for the human eye, therefore, its research potential is quite obvious. Its value as a teaching agent, to allow a permanent record of any unusual fluoroscopic occurrence in a clinical patient, is possibly its greatest contribution. Its clinical applications have been helpful to us thus far in allowing us to differentiate between infundibular stenosis and valvular stenosis in the congenital cyanotic heart group and also in other cardiac defects. We consider it as another method of improved contrast visualization which is now ready and available in the human being. Because cineangiography can be educational, and of research value, I felt it should be discussed along with the contribution of Dr. Goldman.

DR. ARTHUR M. VINEBERG, Montreal.—I should like to congratulate Dr. Goldman on his excellent presentation.

The site at which he has tied the anterior descending branch of the left coronary artery is quite a distance from its origin. A ligature placed in this position fails to include branches which arise proximal to the ligature. When a ligature is placed at the origin of the anterior descending branch of the left coronary artery, there are very few branches that escape and, therefore, very few branches form collateral circulation. There is great variation in the published figures for survival after anterior descending branch ligation. This can be explained by failure of the ligature to include all branches.

In some animals it is impossible to obtain all the branches because occasionally branches arise directly from the trunk of the left coronary artery. Dr. Goldman has demonstrated beautifully how such an artery which has escaped occlusion by the ligature can act as a collateral and revascularize the area formerly supplied by the anterior descending branch. He has further given visual evidence that any survival experiments depending on ligation of the left coronary artery must include a careful inspection of the site of ligation and of the left coronary artery for branches not included in the ligature.

DR. GOLDMAN (Closing).—I am sorry we did not have time to show the technique of direct leads to explore the heart's surface. In answer to Dr. Vineberg's question as to where the collateral coronary vessels are, I do not think it makes a great deal of difference if one ligates at the midportion or at the origin of the anterior descending artery, still the collateral coronary circulation would be present. It appears that it is the pressure in the two coronaries which determines whether or not the collateral circulation will be functional. If the two coronaries are occluded there will not be enough pressure to open collateral circulation. This is clinically borne out because so commonly death results when both coronary arteries are ligated in a dog or if they are occluded by arteriosclerotic processes in human beings. On the other hand, if one artery is occluded, there is good chance that the collateral coronary circulation coming from the other artery will be effective. However, this collateral circulation is not without its limits as we all know from clinical study, and even in the dog it is limited. A small occluded myocardial muscle mass produces often no visible cyanosis and no visible change with fluorescein or in contractility, although there may be electrocardiographic Q or QR waves.

With the direct exploring electrode applied to the surface of the heart it appears that electrical changes which would be brought about by surgically induced coronary circulation could be readily detected. These changes of Q and QR waves should result after experimental ligation of the anterior descending coronary artery. Thus the presence or absence of Q and QR waves after experimental coronary ligation in a prepared dog's beating heart should indicate the effectiveness of the prepared additional surgically induced coronary collateral circulation.

ARTIFICIAL OXYGENATION AND CIRCULATION DURING COMPLETE BY-PASS OF THE HEART

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A KEEN interest in the problems of extracorporeal circulation has been aroused and maintained in many surgeons by the promising results of the experiments of several groups of investigators.[1-5] This interest had, as its background, or was at least nurtured by, the signal advances made in surgery[6-11] in the past fourteen years. In the writings of Kolff, Jongbloed, Gibbon, Miller, and Dennis, physicians have access to excellent summaries of methods of artificial oxygenation and circulation, and to interpretations of correlative, physiologic phenomena.

In this publication, the purpose is to report an experience with the dispersion-oxygenator and pump described by Clark, Gollan, and Gupta.[13] Their heart-lung apparatus employs principles differing from those of the mechanical devices of other investigators.[3, 12] This machine depends upon dispersion for the introduction of oxygen into the blood and for the elimination of carbon dioxide. It provides for the removal of these gases, carbon dioxide, and excess oxygen, in the form of bubbles, before the blood is returned by pump into the animal. The pumping effect of this machine is obtained without the use of roller, diaphragm, or piston systems.

This report, based on the initial experience of the authors, does not deal with many of the problems emphasized by authoritative investigators. It is concerned, on the other hand, with some of the questions confronting a group of workers starting to experiment in this field.

DESCRIPTION AND OPERATION OF THE APPARATUS

Fig. 1 is a diagram of the oxygenation and pumping unit. The venous blood flows from the cannula, draining the superior and inferior vena cavas into the oxygen-dispersion unit, at the base of the apparatus. (*A*, entrance for venous blood.) The first step in oxygenation and in the elimination of carbon dioxide occurs as the blood flows upward in the inner, sintered glass channel of a double-walled Pyrex† chamber. (*C*, double-walled oxygen dispersion chamber.)

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†The three Pyrex units mentioned in the text may be obtained from the Laboratory and Pharmaceutical Sales Division, Corning Glass Works, Corning, New York, designated as Model C, 8 inch dispenser, defoaming chamber and pumping chamber.

The oxygen, which is delivered at a pressure of 5 to 10 pounds per square inch into the glass jacket surrounding the central porous-walled cylinder, passes through the microscopic openings and enters the blood in the form of tiny bubbles. (*B*, entrance for oxygen.) The size of the bubbles is determined by the diameter of the pores (4 to 5 microns) in the wall of the central cylinder and possibly by the surface tension of the blood. The surface of the sintered glass must be wettable by blood. A hydroprobic, porous surface produces large

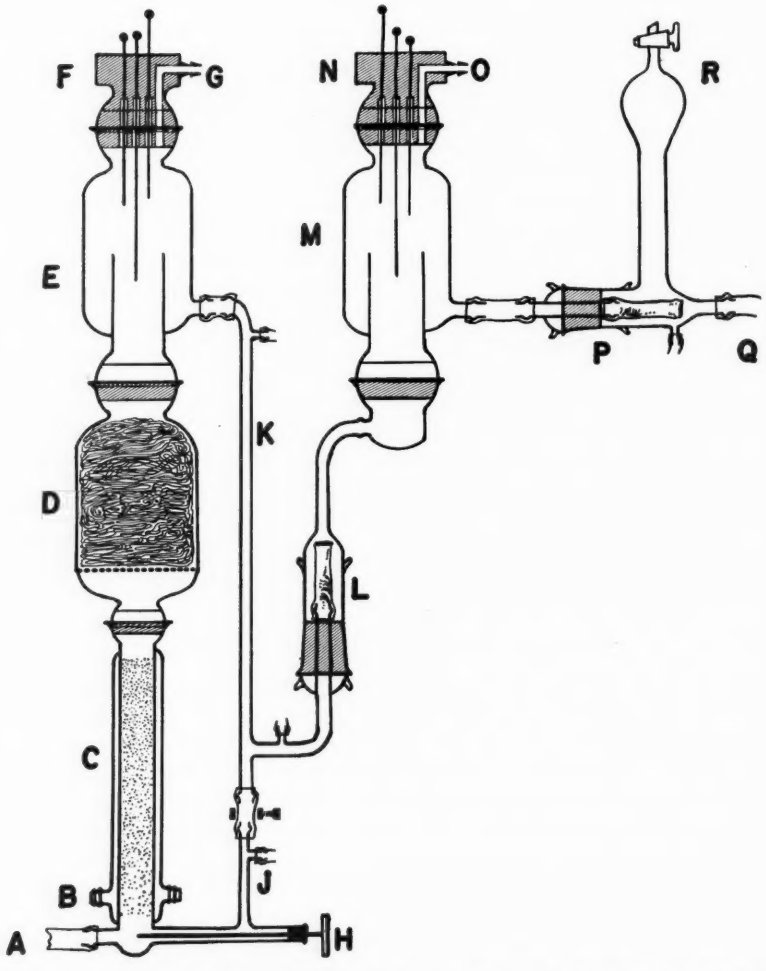

Fig. 1.—*A*, Entrance for venous blood; *B*, oxygen entrance into outer jacket; *C*, double-walled oxygen dispersion unit; *D*, coalescence chamber; *E*, reservoir; *F*, electrode holder; *G*, attachment for suction line; *H*, thermometer; *J*, by-pass channel for venous blood; *K*, channel for arterialized blood; *L*, valve; *M*, pumping chamber; *N*, electrode holder; *O*, attachment for suction-pressure line; *P*, valve; *Q*, outlet for arterial blood; *R*, "elastic" chamber.

bubbles, which are less efficient than small ones in this process of oxygen and carbon dioxide exchange.

The blood must be freed of these tiny bubbles (excess oxygen and carbon dioxide) before it can be pumped back into the animal's vascular system. This second step in the extracorporeal circuit is completed in the Pyrex coalescence chamber, which is sealed to the upper end of the oxygen-dispersion unit. (*D*, coalescence chamber.) In this chamber the fine mist of tiny bubbles coalesce to form large bubbles which are easily withdrawn from the apparatus. Bubble coalescence is obtained by passing the blood over a broad surface coated with polymethylsiloxane defoaming compound (DC Antifoam A).* The coalescence chamber is packed with fine polyethylene fiber which is coated by 2 Gm. of Antifoam A, evaporated from an ether solution. To date, experiments with this organo-silicon oxide have shown it to be innocuous.[14]

The large bubbles and the blood, the latter enriched with oxygen and freed of some of its carbon dioxide, continue their upward course from the coalescence chamber to enter the third stage of the extracorporeal circuit. The glass chamber used for this step is the third in the vertical line, and serves as a reservoir and avenue for the elimination of bubbles. (*E*, reservoir.) The large bubbles then leave the surface of the blood and are removed by the suction to which this chamber is exposed. (*G*, attachment for suction line.) The intermittent suction effect is controlled by an electrode projecting at an upper level in the chamber. A minute current flows through this electrode when the blood level rises high enough to contact it. The current causes a solenoid to interrupt the suction for as long as the electrical circuit is complete.

The fourth step in the extracorporeal course of the blood is the process of pumping it back into the vascular system of the animal. The specifications of the Pyrex pumping chamber are the same as those for the reservoir. (*M*, pumping chamber.) Pumping is done by the alternation of suction and pressure over the surface of the blood in this chamber. (*O*, attachment for suction-pressure line.) No moving parts are in contact with the blood in a pump employing this principle. This pulsating action is controlled by two electrodes supported at different levels in the upper half of the chamber. A very small current flows through each electrode when blood rises high enough to contact it. This current causes the solenoids in the suction and pressure lines to open and close at the appropriate moments. When the blood level rises high enough to touch the end of the upper electrode, the suction is interrupted and the pressure phase begins. When the blood level falls away from the tip of the lower electrode, the pressure is discontinued and suction is once more applied.

A narrow by-pass channel, with an adjustable clamp, serves to shunt venous blood from below the oxygen-dispersion unit into the stream of "arterialized" blood before it enters the pumping chamber for return to the animal. (*J*, by-pass channel; *K*, channel for "arterialized" blood flowing to pumping chamber.) The volume of blood shunted around the first three steps of the circuit may be

*Made by Dow Corning Company, Midland, Mich.

varied by adjusting the screw clamp on the tubing in the by-pass line. The shunting of *some* venous blood into the arterialized stream serves to counterbalance any excessive oxygenation which develops in the oxygen-dispersion unit. The blood temperature is measured directly by a thermometer (*H*) which projects into the stream entering the system.

The Pyrex "elastic" chamber (*R*) buffers the pulsating stream from the pumping chamber. The elastic unit maintains some pressure effect on the arterial stream while the pumping chamber is refilling in the suction phase. (*Q*, outlet for arterial blood.) The flow rate is increased by this effect.

The only two valves (*P* and *L*) in the entire system are the simplest type and are made of Silastic in the shape of flat tubing.* The electrodes are stainless steel rods, which are easily adjusted up or down in their Lucite holders (*F* and *N*). Only 5 to 10 microamperes flow through these electrodes when the circuit is completed by contact with the surface of the blood. The current of 10 microamperes does not cause any damage to the blood in the circuit. Except for the porous unit for oxygen-dispersion, all the glass parts and the plastic tubing (Surgical Koroseal or Tygon S-22-1) used for making connections are coated with silicone. This is done by wetting the parts and tubing with a 3 per cent benzene solution of DC-1107,* allowing them to dry, and baking them for several hours at 150° C. The coating is reapplied after 20 experiments, or when the surfaces no longer appear hydrophobic.

A satisfactory source of suction and pressure may be found in a variety of standard pieces of laboratory equipment. (The Whirlwind machine† was used as the source of suction in these experiments.) The pressure for pumping was obtained from a tank of oxygen.

The assembled apparatus is put through a test run after all the parts have been securely joined together; during this period, the pressure on the pumping line is increased gradually to 14 pounds per square inch, a pressure which exceeds that used in arterial perfusions. The vacuum pump is adjusted so that the suction is between 6 and 10 inches of mercury. The oxygen pressure in the outer jacket of the dispersion unit is increased, until a mistlike current of bubbles is seen entering the coalescence chamber and an excess of the gas starts escaping from the surface of the liquid in the reservoir. The pumping rate is controlled by regulating the clamp on the suction-pressure line; or, if desired, the rate may be controlled by regulating a clamp on the arterial line leading from Q (Fig. 1).

In cleaning the apparatus, saline is first circulated through it, then water, and finally water containing household "chlorine water." The parts are completely disassembled and individually washed and dried. The polyethylene fiber in the coalescence chamber is cleansed by rinsing with water, then with 95 per cent alcohol, and finally with ether in order to remove the antifoam compound. The coalescence unit may then be allowed to dry, or the polyethylene fiber may be recoated immediately with antifoam compound. The porous glass wall in the oxygen-dispersion unit requires meticulous cleansing. For a thorough

*Made by Dow Corning Company, Midland, Mich.
†Obtained from Max Wocher and Company, Cincinnati, Ohio.

rinsing of the sintered surface, a stream of strong chlorine water is passed into the oxygen inlet of the outer jacket. The unit then stands overnight in concentrated sulfuric acid, to which a few crystals of sodium nitrite have been added. This acid is removed by drawing a 5 per cent solution of sodium bicarbonate through the porous wall.

The entire apparatus and its supporting frame of aluminum rods can be placed on its side in an autoclave of standard size. This method of sterilization has no adverse effect upon the plastic tubing, which is used to join the chambers and for attaching the machine to the cannulas inserted in the animal. The Silastic valves and the Lucite electrode holders are not altered by autoclaving. It is necessary, however, to sterilize the polyethylene fiber-filled coalescence chamber by soaking it in a germicidal solution.

OPERATIVE PROCEDURE

The animals used in this series were all mongrel dogs between 1 and 3 years of age, varying in weight between 30 and 35 pounds. Each animal was observed for 2 to 4 days pre-operatively, and an estimate of cerebral function and normal activity was made for comparison with the condition following total by-pass of the heart and lungs.

Although the apparatus used fits into a standard autoclave, no attempt was made in any of the experiments to adhere to aseptic surgical procedure. The animals were shaved and washed prior to surgery, in order to eliminate as much gross contamination as possible; but none of the drapes, instruments, and equipment were sterilized.

The animal selected for pumping was premedicated with morphine and atropine prior to the intravenous administration of Pentobarbital Sodium. Large operative wounds for the exposure of the heart and great vessels in animals whose blood is rendered incoagulable by heparin, as in these experiments, necessitated meticulous attention to possible sources of bleeding during the operative procedure. No tissue encountered in the dissection was divided without first being clamped. The small portions of tissue on each side of the proposed line of division were divided, and each of these bundles was individually ligated. The right pleural cavity was entered through the fourth intercostal space; and the femoral arteries, femoral veins and the right common carotid were dissected free for a distance long enough to permit cannulation.

When the chest of the animal was opened, controlled pressure was applied to the breathing bag attached to the endotracheal tube. The rib margins were separated with a self-retaining retractor, and the right lung was displaced so as to expose the superior vena cava. The azygos vein was divided and the pericardium was opened, in order to expose the right auricle and the inferior vena cava. A rubber ribbon was passed around the superior and inferior vena cavas, at their entrance into the right auricle. A measured dose of heparin was then given intravenously, and the peripheral cannulations carried out. When the animal was ready for total by-pass of the heart and lungs, the two rubber ribbons around the superior and inferior vena cavas were tightened around the limbs of

the right heart cannula. This tightening effectively prevented the return of venous blood to the right heart from the peripheral circulation. During the period of total by-pass, an incision was made in the right auricular appendage to permit exploration, under direct vision, of the interior of the right auricle. The venous return in the coronary sinus was drawn off by a simple suction device and was then measured. (The presence of air in the venous pick-up line of a dispersion-oxygenator is of no consequence; therefore, this blood can be returned to the venous side of the appartus.)

Anticoagulants.—In the first eight experiments, the donor blood, for filling the machine and for replacing blood lost from the incisions in the recipient animal, was collected in standard transfusion bottles containing 120 c.c. of ACD solution. When this blood was pumped into recipient dogs there was a rapid and irreversible fall in blood pressure. Donor blood was therefore collected, with heparin as the anticoagulant (50 mg. per 1500 c.c. of blood).

In the first 33 experiments, the recipient animals were given heparin in dosages of 3 to 4 mg. per kilogram of body weight, just prior to the insertion of the cannulas. This dosage was adequate for maintaining an incoagulable state during the pumping period. However, near the end of the pumping period, small collections of material thought to be fibrin were noted on the walls of the pumping chamber. The heparin dosage was revised upward until the formation of this material ceased. Prior to cannulation, all the dogs in the remainder of the series received 10 mg. of heparin per kilogram of body weight.

Reversal of the heparin effect at the conclusion of circulation through the experimental circuit remained an unsolved problem. Many of the first animals received protamine sulfate in doses of the number of milligrams equal to the amount of heparin injected. Some of these animals suffered severe hypotension on administration of protamine, even when this was given very slowly and in high dilution. Transfusion of fresh, whole blood, collected in a siliconed syringe from a donor dog, seemed to be more effective in reversing the heparin effect. This approach to the clotting problem, although not ideal, proved effective enough to permit eliminating the use of protamine in many dogs later in the series.

Eight animals in the entire series died of postoperative hemothorax, and fatal bleeding seemed to have come from the region of dissection in the mediastinum. This bleeding developed in spite of the meticulous ligation of all bundles as the tissues were divided. However, only two of the final 23 dogs used in the series died of uncontrolled oozing. This reduction of mortality from postoperative hemorrhage was attributed to two factors—the liberal use of fresh, whole blood, and the use of the multiple ligation technique.

Cannulation.—An L-shaped polyethylene tube, similar to the cannula described by Leeds,[15] was used in the first 42 experiments for the collection of the venous blood returning to the right auricle from the superior and inferior vena cavas. This tube was inserted into the superior vena cava through the proximal end of the divided azygos vein, and down into the inferior vena cava through the right auricle; the stump of the azygos vein was then ligated about

the stem of the cannula. In the course of these 42 experiments, three serious faults in this system were observed. First, the venous return was often inadequate to maintain a satisfactory flow rate. This occurred because of a tendency for the walls of the superior and inferior vena cavas to pull into the openings of the cannula during the suction period of the pumping cycle, and to effectively block the cannula. Second, the insertion of such a cannula was attended by the risk of introducing air into the right auricle. Third, the upright limb of the cannula blocked direct operative approach to the heart.

The problem of venous return through a cannula inserted into the superior and inferior vena cavas through the right auricle was managed at first by the incorporation of a suction-release mechanism. Through this device, the suction was automatically turned off when the indrawn walls of the superior and inferior vena cavas blocked the cannula. Flow rates were increased by this mechanism, but were still not the best obtainable.

Rapid, continuous flow of venous blood into the machine was eventually obtained by the use of a "femoral vein supplement." This consisted of a long polyethylene catheter with multiple perforations in its wall. The catheter was passed into the inferior vena cava through a femoral vein, and was threaded through the intracardiac portion of the L cannula into the superior vena cava. The end of the "femoral vein supplement" catheter, which remained protruding from the femoral vein, was sealed to prevent blood from escaping and air from entering. The small, indwelling, perforated catheter made it mechanically impossible for the walls of the superior and inferior vena cavas to collapse completely. Through this device there was uninterrupted filling of the machine, and flow rates between 2,500 and 3,000 c.c. per minute were easily obtained.

The danger of air embolism during the insertion of the cannula was eliminated by the use of a Cellophane dialysis-tubing obturator in the lumen of the cannula. A length of Cellophane tubing was closed at one end, and its outer surface was lubricated with a small amount of mineral oil in order to facilitate removal. It was then inserted into the L cannula and distended with saline. The Cellophane sausage thus formed occluded the lumen completely, and permitted insertion of the right heart cannula without danger of air embolism or hemorrhage. When the cannula was in place, the oiled obturator was removed, and its pistonlike action on removal filled the cannula with blood.

At the termination of total by-pass, closure of the heart and removal of the right heart cannula were accompanied by the danger of air embolism. The possibility of trapping air in the opened heart was reduced by allowing the heart to fill completely, before closure, with blood from the coronary sinus,[4] or by pouring in saline to fill the auricle. The danger of air embolism during the removal of the L cannula was minimized by filling the pleural space with saline, withdrawing the instrument, and clamping the vein under the level of this solution.[16]

Several methods for the return of oxygenated blood to the animal were evaluated. In early experiments, oxygenated blood was returned through both femoral arteries in a retrograde fashion by the use of polyethylene catheters

passed into the arch of the aorta. Arterial return by this method was adequate, but high pumping pressures were necessary in order to overcome the resistance in long catheters. Return of oxygenated blood was attempted through one femoral artery catheter and one common carotid artery cannulated with a T tube, so that both limbs of the divided carotid artery functioned as arterial in-

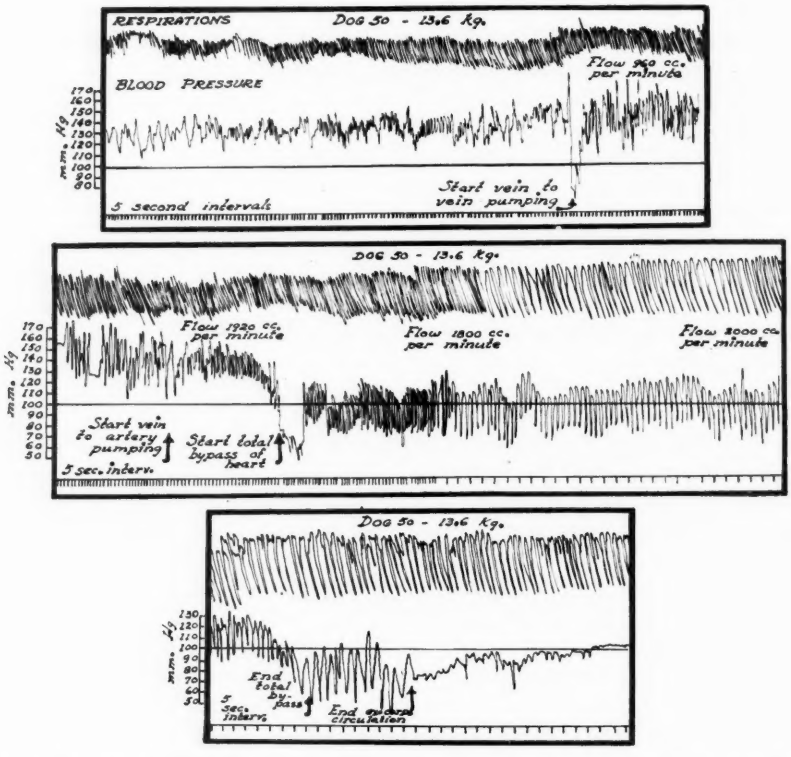

Fig. 2.—Portions of records of Dog 50. Tracing of respirations and blood pressure with flow rate and changes in extracorporeal circuit.

lets. This was discontinued because orbital edema on the same side seemed to result. In the most recent 20 experiments, the arterial return was carried through two polyethylene cannulas. One was pointed centrally in the right femoral artery, and the other was pointed toward the heart in the right common carotid artery. These cannulas were 4 mm. in diameter, and were inserted for only short distances.

Two additional cannulations completed the pick-up and return systems. A catheter was placed in the right femoral vein, and this served as a channel for return during vein-to-vein pumping. In order to record blood pressure and to obtain samples for oximetry, the left femoral artery was cannulated.

By-Pass of the Heart.—After the right heart cannula was connected to the venous pick-up tube and the arterial inlet connections were made, the pump was turned on. For the first few minutes, the blood was drawn out through the right heart cannula, oxygenated, and returned through one femoral vein. (This was the period of vein-to-vein pumping indicated on Figs. 2 and 3.)

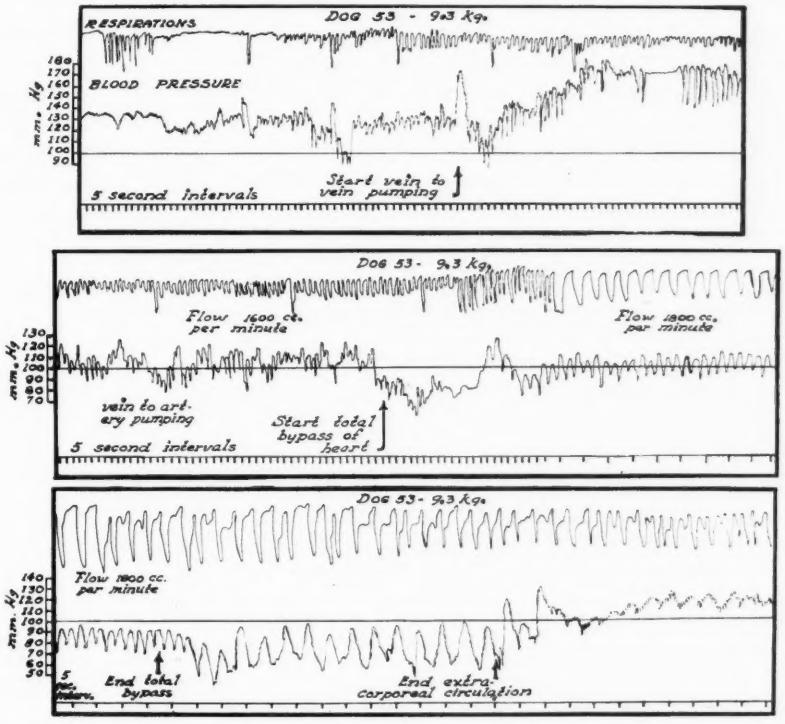

Fig. 3.—Portions of record of Dog 53. Tracing of respirations and blood pressure with flow rate and changes in extracorporeal circuit.

When a satisfactory level of oxygenation was established, the femoral vein was closed and the cannulas in the femoral and carotid artery were opened. This vein-to-artery, partial by-pass was continued for a short period, during which time mechanical adjustments were made. The two rubber ribbons about the superior and inferior vena cavas were then tightened so as to compress the cavas around the stem of the right auricle cannula. This established the total by-pass phase of the experiment, and from this time on until the end of the by-pass, the apparatus functioned with very few further adjustments.

OBSERVATIONS AND LABORATORY DATA

Continuous recording of the blood pressure, respirations, electrocardiogram, body temperature, and urine formation was attempted in most of the experi-

ments. For the most part, it is practicable here to refer only to the observations recorded in that phase of the experiment when the animal was on total by-pass of the heart. Portions of the records of two experiments are shown in Figs. 2 and 3. The following laboratory data cited, however, cover the full duration of each experiment and not just the crucial 30-minute period of total cardiac exclusion.

The mean blood pressure remained within a normal range in most of the animals during total by-pass. With regard to the breathing, it is impossible to say more than that the animals continued with normal respiratory movements, even when, in total by-pass, the lungs were deflated and pale, and practically bloodless. After all the blood returning through the superior and inferior vena cavas had been rerouted through the apparatus, the volume of the heart decreased immediately and the auricles were quite collapsed. During this same period,

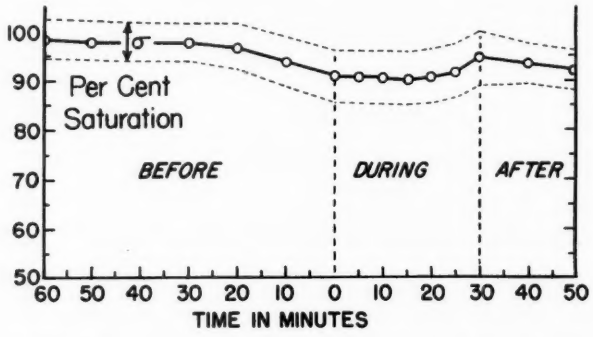

Fig. 4.—Oxygen saturation of arterial samples during total by-pass. The open circles represent the mean values obtained. Each of these averages is derived from twelve to eighteen analyses in the early period before pumping. In the period immediately before, during, and after the by-pass, between 25 and 35 analyses were averaged for each point. In the late period after by-pass, between eight and thirteen analyses were averaged for each point. Each figure records the analyses of a total of 325 arterial samples. The standard deviation from the mean is indicated by the dotted lines, and is obtained by the following formula: $\sigma = \sqrt{\left(\frac{1}{N}\right)(\Sigma X^2) - M_{x2}}$

the ventricular contractions remained strong and tended to slow down. There was no gross disturbance in the electrocardiogram, and in a few experiments, the animal had an occasional ventricular extrasystole. With the wall of the right auricle opened wide, the return from the coronary veins, collected by direct aspiration of the coronary sinus in several animals, measured 30 to 40 c.c. per minute. The body temperature was allowed to fall to subnormal levels (32° to 36° C.) throughout many of the experiments. In the latest group, the body temperature was held at a nearly normal level (36° to 38° C.) by adding a heating coil to the oxygenating unit and by decreasing radiant heat loss from the animal. The formation of urine did not seem to be interrupted in the total by-pass phase of the experiment. The survivors often regained consciousness at the time of closure of the chest wall incision, and within four hours after completion of the experiment they stood on all fours and started to drink water.

The oxygen saturation of arterial samples ranged between 93 and 98 per cent in the control period before pumping (Fig. 4). During the total by-pass of heart and lungs, the oxygen saturation averaged between 90 and 95 per cent. After restoration of normal circulation, oxygen saturation in arterial samples varied between averages of 90 and 93 per cent. At no time in the interval of total by-pass did the averages of arterial saturation fall below 90 per cent.

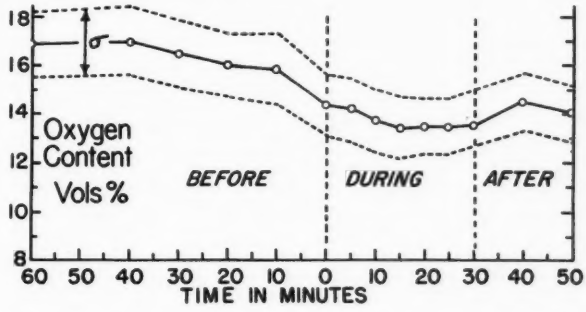

Fig. 5.—Oxygen content of arterial samples during total by-pass. *(For further explanation, see Fig. 4.)*

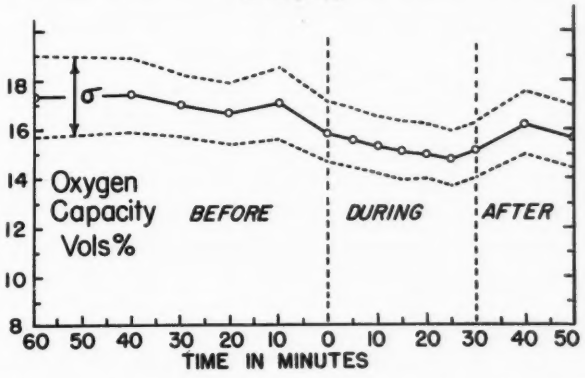

Fig. 6.—Oxygen capacity of arterial samples during total by-pass. *(For further explanation, see Fig. 4.)*

The oxygen content of the arterial blood shown graphically in Fig. 5 was reduced slightly during the by-pass period. This change was due in part to the addition of fluids not containing hemoglobin (physiologic saline solution, 5 per cent glucose in water, etc.). That this was a factor was indicated by the fall in oxygen capacity which occurred at the same time (Fig. 6). Both oxygen content and capacity rose somewhat after the conclusion of by-pass, probably as the result of transfusions of whole blood.

Prior to the period of artificial oxygenation, arterial samples varied considerably in their total carbon dioxide content, as shown in Fig. 7. This probably resulted from variations in the method of anesthetizing and of administering oxygen. The total carbon dioxide content was increased in arterial samples

taken during the by-pass period. After the pumping, the trend of the total bicarbonate was downward and approaching control levels. A carbon dioxide-absorbing unit was inserted in the line (Fig. 1, *G*), through which all of the carbon dioxide and excess oxygen were withdrawn from the system. By this absorption unit it was possible to use a gravimetric method for measuring the amount of carbon dioxide eliminated in the process of dispersion-oxygenation. The average in six experiments was 40.3 c.c. per minute during the period of total by-pass.

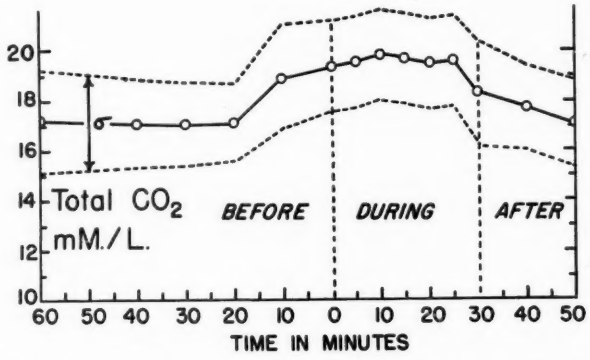

Fig. 7.—Total carbon dioxide content of arterial samples during total by-pass. *(For further explanation, see Fig. 4.)*

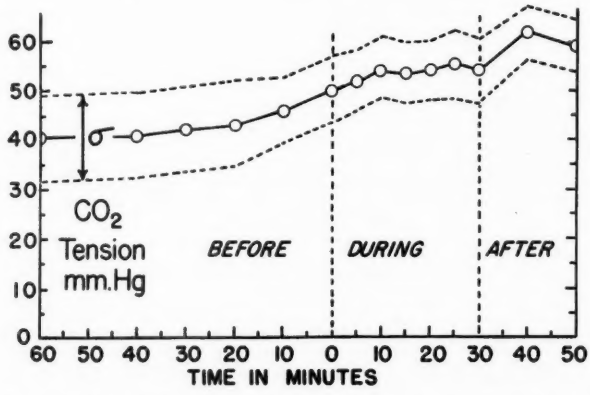

Fig. 8.—Carbon dioxide tension of arterial samples during total by-pass. *(For further explanation, see Fig. 4.)*

Analysis of arterial blood drawn before extracorporeal circulation was started showed a tendency for the carbon dioxide tension to rise (Fig. 8). This tendency was accentuated after pumping was started, with the values remaining at about 54 mm. Hg during the remainder of the period of complete by-pass. Following the period of by-pass, the carbon dioxide tension rose somewhat higher.

During the prepumping period of the experiments the plasma pH gradually fell, as shown in Fig. 9. This change was probably due to retention of carbon dioxide, resulting from the method of anesthetization and inflation of the lungs. During the by-pass period, the tendency toward acidosis was somewhat aggravated. In the postpumping period the pH fell further.

The criteria of survival were based on observations made in the period immediately following total by-pass. No animal was considered a survivor unless it made a complete recovery from the anesthetic, evidenced good cerebral function, walked, ate, drank, voided, and defecated. Liberal doses of antibiotics were administered, but long-term survivors were few. Only seven of these animals lived for several months before they were sacrificed; the others that had met the criteria of survival succumbed to intrathoracic and generalized infection or to thrombosis of the superior vena cava, in a period of forty-eight hours to two weeks (See Table I).

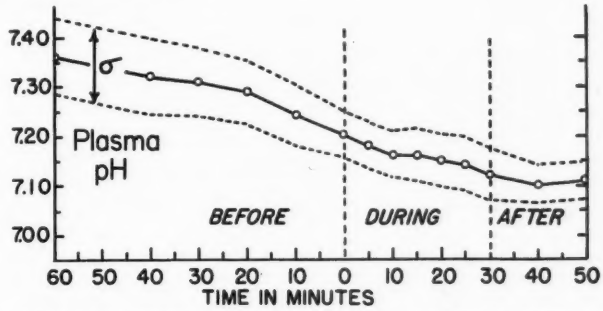

Fig. 9.—The pH of arterial samples during total by-pass. *(For further explanation, see Fig. 4.)*

TABLE I. ANIMALS THAT MET CRITERIA OF SURVIVAL

DOG. NO.	DATE OF BY-PASS	DATE OF DEATH	REMARKS
8	5/26/51	8/ 3/51	Sacrificed. Normal autopsy.
12	7/ 7/51	9/17/51	Sacrificed. Dense right-sided pleural adhesions.
16	7/26/51	9/ 9/51	Sacrificed. Pericardial effusion and subcutaneous abscesses in chest wall.
17	7/27/51	9/ 9/51	Sacrificed. Normal autopsy.
21	9/ 1/51	10/15/51	Died. Chylothorax and compression atelectasis.
37	11/10/51	------	Living.
38	11/11/51	11/14/51	Died. Marked pulmonary consolidation.
41	11/24/51	11/26/51	Died. Thrombosis of the superior vena cava.
45	12/22/51	12/24/51	Died. Marked pulmonary consolidation and edema.
47	12/29/51	1/11/52	Accidentally electrocuted.
50	1/ 6/52	------	Living.
51	1/12/52	1/13/52	Died. Pulmonary consolidation and edema.
52	1/13/52	1/14/52	Died. Thrombosis of the superior vena cava.
53	1/19/52	2/ 2/52	Died. Multiple abscesses and purulent pericarditis.
55	1/26/52	2/ 3/52	Died. Thrombosis of the superior vena cava.
56	1/27/52	1/29/52	Died. Marked pulmonary consolidation and edema.

Of the 57 dogs subjected to complete by-pass of the heart and lungs for periods of thirty to forty minutes, 52 remained alive until the extracorporeal circulation was completed. The first animal to meet the criteria of survival was the one studied in the eighth experiment. Consecutive surviving animals were obtained after 50 experiments had been completed. Sixteen dogs made complete recoveries, giving an over-all survival rate of 28.7 per cent. The initial survival rate with citrated blood for transfusion was 12 per cent on the first eight animals. The rate of survival rose to 33.3 per cent after the citrate solution in the transfusion blood was replaced by heparin as an anticoagulant. After a careful technique was instituted of crossmatching donor and recipient animals, the survival rate rose to 40 per cent. The introduction into the apparatus of a by-pass channel, which shunts a fraction of the venous blood directly into the chamber pumping out the arterial return, resulted in further improvement in the survival rate; 57 per cent of the last fourteen animals survived.

COMMENTS

From this experience with extracorporeal oxygenation and pumping of the blood, there are some observations which merit further comment. These observations are related, it is believed, to factors determining the success of this apparatus and method, and are therefore discussed in the following text.

Crossmatching Donor and Recipient Dogs.—There is little doubt that the transfusion of incompatible blood caused the death of some of the animals early in the experiment. The first 29 experiments were carried out without regard for the possibility of blood incompatibility among dogs. After this, using the direct slide method, the recipient's cells were always matched with plasma from the prospective donors.[17] (Approximately 25 per cent of the tests showed strong agglutination.) Ancillary experiments were carried out in which heparinized blood known to be incompatible was given as replacement transfusions to two dogs. The first animal became hypotensive and died within twenty minutes. The second remained anuric and died after twenty-four hours. The autopsy findings in both animals were renal ischemia and infarction, and severe pulmonary edema.

Carbon Dioxide Elimination.—It has been suggested that the reduction of serum pH and elevation of carbon dioxide tension may have harmful effects on dogs subjected to total by-pass of the heart and lungs.[18] The possible significance of these changes was considered in the analysis of the early experiments in which the dogs succumbed. Collateral studies were made with three dogs rebreathing carbon dioxide in an oxygen-filled bag. The pH of their arterial blood was followed by frequent determinations with a Beckman pH meter. Ten minutes after the start of rebreathing the pH fell from normal to 7.2. After eighteen minutes the pH was 7.11. For thirty minutes, the animals remained with an arterial pH of 6.90 to 7.13. Following this period they recovered from their anesthetic without delay, and were normal in all respects. It is known that an arterial pH, if severely reduced for two to three hours, may cause death in dogs.[19] However, the severe acidosis, if present for relatively short periods, may not have a harmful effect.

Filters in the Extracorporeal Circuit.—Fine mesh, stainless steel and sintered glass filters were employed in some of the experiments. These porous surfaces caught some small clumps of erythrocytes and fibrin masses, but it was difficult to ascertain that the filtering surface was not a factor in the formation of these tiny, unshaped groups. With the increased dose of heparin employed in the most recent experiments and with the crossmatching technique, need for a filter was probably reduced. All except three of the surviving animals were maintained without a filter in their extracorporeal circuit.

Thrombosis of the Superior Vena Cava.—Thrombosis of the superior vena cava was the cause of death in three dogs that had made complete recovery from the period of total by-pass. The following are the factors responsible for these thromboses, which were all at or above the level of the azygos vein and never in the inferior vena cava: first, trauma to the intima of the superior vena cava during cannulation, and while the walls of the vena cavas were pressed to the cannula in the period of total by-pass; second, the intravenous administration of protamine sulfate into the cephalic vein, relatively close to the site of caval trauma and the stump of the azygos vein; third, local bacterial infection in animals, with septicemia and abrasions of the intima of the superior vena cava.

With some practice, the cannula can be inserted without intimal trauma. Narrow rubber ribbons have been employed as ligatures, to compress the caval walls around the instrument for the period of total venous drainage. Tight ligation with a cord, with its resultant ischemia of the vessel wall, is avoided as much as possible.

Autopsy Findings on Dogs That Succumbed.—A study of the results of necropsy on animals that survived for only a few hours after the total by-pass, did not always reveal the cause of death. The brain was not examined in most instances, and no gross abnormality was identified in the brains that were removed. It was noted, however, that a large proportion of the dying animals exhibited signs usually associated with cerebral anoxia in man.

A variable amount of pulmonary interstitial and peribronchial bleeding was a frequent finding. This gave the appearance of a red consolidation of the lung. (Microscopic sections disclosed hemorrhage and edema.) The application of excessive pressure in a closed system for the administration of oxygen into the trachea during stages of the operation, is possibly one factor in the pathogenesis of this hemorrhage. A second factor may be the accidental needle puncture of the lung in a heparinized animal during thoracenteses carried out in the post-operative period.

In the gross, the kidneys were usually normal in size and color, with well differentiated cortical and medullary portions. On the surface of many of the kidneys examined, however, there were one or more small, cortical infarcts. These ranged from 2 to 5 mm. in diameter. The microscopic sections revealed infarcted tissue and degeneration of all cellular elements.

SUMMARY

1. A description is given of a simple, all glass dispersion-oxygenator with some of its effects on the blood flowing through the extracorporeal circuit.

2. The operative procedure for the experiments, the use of anticoagulants, and special methods of cannulation are given in detail.

3. Observations made during by-pass of the heart and lungs are listed; analysis of arterial samples for the oxygen and carbon dioxide content and pH is also included.

4. Experiments on 57 dogs are described, in which there was total by-pass for not less than 30 minutes. (Fifty-two of these animals remained alive for the duration of the experiment.) Survival with complete recovery from the anesthetic is emphasized, and 16 animals in this category are cited.

5. Several specific problems associated with extracorporeal oxygenation and pumping of blood are discussed briefly.

The authors wish to express their gratitude to Dr. Sol Kaplan, Dr. Frank Gollan, and Dr. Frederic Silverman for their advice and assistance with many of the fundamental problems encountered. The completion of the study would not have been possible without the unlimited technical assistance of Miss Molly MacKenzie and Miss Ruth Parker. The Department of Anesthesia of the Cincinnati General Hospital, under the direction of Miss Mary Alice Costello, was most helpful throughout the entire program.

Mr. Fred Hooven of Dayton, Ohio, gave invaluable assistance by his advice on problems in electronics. The technical assistance of Mr. Dean Kimball of Dayton is also acknowledged with appreciation. Through the Vernet Equipment Foundation of Antioch College, valuable pieces of recording equipment were made available for use in the investigation.

The authors are especially indebted to Mr. H. E. Elwood of the Corning Glass Works, Corning, New York, Dr. Shailer Bass of Dow Corning Company, Midland, Michigan, and Dr. K. W. Thompson of Organon, Orange, New Jersey. The material assistance and technical advice from each of these men and their companies made possible the continuation of this work.

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(For discussion, see page 151.)

SOME PHYSIOLOGIC ASPECTS OF THE ARTIFICIAL HEART PROBLEM

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SEVERAL investigators have reported on various types of artificial hearts, to by-pass the heart, either partially or totally. These investigations have been along two lines: first, total by-passing of the entire heart and lungs such as reported by Gibbon and associates[1] or Dennis and associates;[2] second, the unilateral substitution for one or the other sides of the heart while the other side and the lungs continue to function. Leeds, Puciss, and Siegel[3] as well as Sewell and Glenn[4] have reported substitutions for the right side of the heart. Sirak, Edison, and Zollinger[5] as well as Kantrowitz and Kantrowitz[6] have reported substitutions for the left side of the heart.

There have been few artificial mechanisms reported which would perform any or all of these functions. Wesolowski and Welch[7] have reported an artificial mechanism whereby either side of the heart or both sides could be by-passed using the lungs as the oxygenator. It is not the purpose of this manuscript to review all the various artificial mechanisms that have been reported to date. We wish to present, however, some physiologic data which probably pertain to all types of artificial mechanisms.

Analyses of several types of pumps that have given some promise of being satisfactory for maintaining the systemic circulation were made at the beginning of our investigation. The Dale-Schuster pump was selected for further analysis and testing because of certain inherent features. This type is a variable displacement pump, that is, each stroke of the pump is accompanied by discharge of a quantity of fluid governed by the actuating pressure and resistance to fluid flow in the circulatory system.

Pumping action in the Dale-Schuster pump is obtained by creating a volume change in a latex rubber finger cot which is enclosed in a cylinder (Fig. 1). The finger cot also separates the actuating air from the fluid being pumped. Volume change of the finger cot is achieved by collapsing it with negative air pressure and then expanding it with positive air pressure. Collapse of the finger cot results in liquid being drawn into the cylinder through the inlet valve located in the valve body. Expansion of the finger cot forces the liquid out of the cylinder through the outlet valve. The inlet and outlet valves are closed by pressure to provide unidirectional flow of the blood.

The artificial heart mechanism reported here was made for us by the Research Laboratories Division, General Motors Corporation. The viscosity studies were also made by them.

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From The Research Division of Harper Hospital.

Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery, Dallas, Texas, May 8-10, 1952.

Positive and negative air pressures are admitted alternately to the finger cot by an air valve which can be operated at different speeds. Air pressure control is obtained by use of a pressure regulator and an air-bleed valve. The maximum pressure that can be applied to the blood is the actuating pressure, providing the valves are properly designed to prevent high localized pressures at the seats when they close.

After extensive tests conducted with water to determine operating characteristics of this single pump unit, tests were run to determine the amount of hemolysis caused by the pump. No significant hemolysis of the blood occurred over comparatively short periods of circulation.

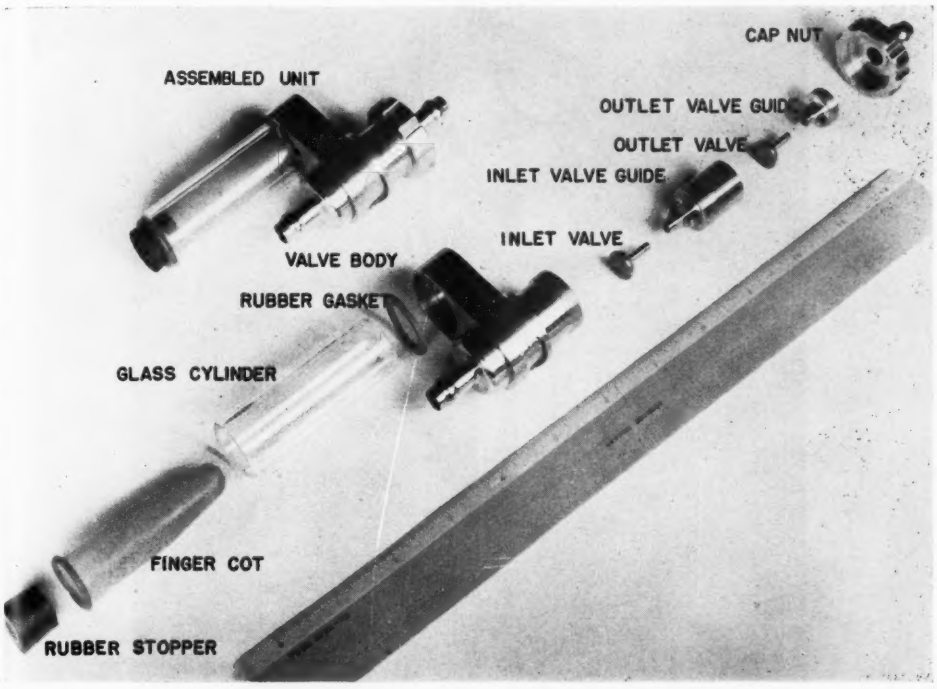


Fig. 1.—Individual pumping cylinder.

Since our tests on this single unit gave such good results, our next step was to design a unit with sufficient capacity to accommodate an average-size adult and enough flexibility to fit the proposed medical research program. The proposed program to be followed in application of the artificial heart consisted of four steps: (1) substitution for the right heart, (2) substitution for the left heart, (3) substitution for both sides of the heart still using the lungs, and (4) substitution for both sides of the heart using an artificial lung. In other words, the mechanical heart should have two independent pumps, one to take the place of the right heart and the other to take the place of the left heart.

The peak pressure required to pump a given quantity of fluid under continuous flow conditions is less than the peak pressure required to pump the same given quantity of fluid under pulsating flow conditions. In order to minimize the blood pressure delivered to the lungs, a continuous flow pump was designed for the right side (Fig. 2). To achieve a higher blood pressure in the arterial system, the left side of the mechanical heart was designed to a pulsatile flow. Sufficient pump capacity to handle a normal adult was obtained

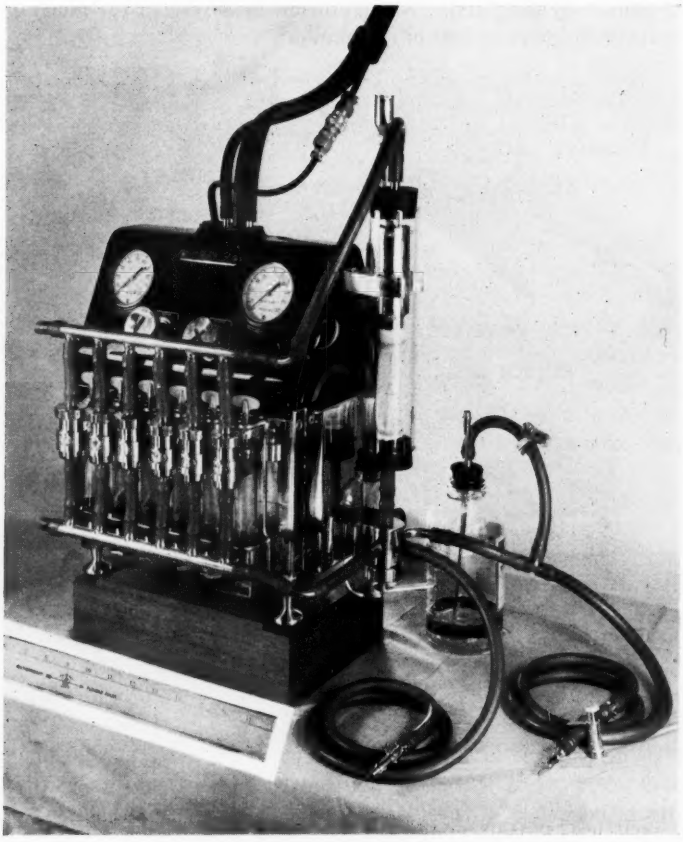


Fig. 2.—Right side of assembled pump.

by using six individual units operating in parallel on each side. Constant flow on the right side was obtained by valving the admittance of air pressure to the inside of the finger cots in such a manner that one of the six individual pumps discharged every 60 degrees of camshaft rotation. The camshaft is common to both sides and it operates lever arms which valve the air pressure to the different pumps. The cams on this shaft are designed to admit positive and negative

pressures for equal periods of time to the finger cots. In order to add more flexibility to the mechanical heart, three camshaft speeds of 65, 75, and 85 revolutions per minute were made available by use of a step pulley arrangement. Separate controls for positive and negative air pressures are provided for each side.

Any number of units, from one to six, can be used on either side. The number used is governed by the required capacity. Our experience indicates that three units have more than ample capacity for animals weighing 20 kilo-

Fig. 3.—Power supply for mechanical heart.

grams when using 8 mm. tubing for connections to the cannulae. Use of 12 mm. tubing with six units will give the pump a capacity of approximately 5 liters per minute.

Pump parts are made of stainless steel, glass, and rubber. Standard Pyrex brand glass is used for the glass parts while the finger cots are made out of surgical latex rubber.

Individual units are very easy to disassemble for cleaning and autoclaving. All surfaces that come in direct contact with the blood stream are coated with

Dow Corning DC-1107 Silicone dissolved in carbon tetrachloride. A 2 per cent by volume solution of DC-1107 Silicone in carbon tetrachloride is used. After coating, the metal and glass parts are baked for 1 hour at 300° F. Since the Silicone coating makes the surfaces practically nonwettable, it is felt that this helps to prevent the formation of fibrin as the blood passes through the pump.

In order to measure the blood flow during operations, a Weir type flow meter was made (Fig. 2). The flow rate in this meter is a function of the blood level as it discharges through a vertical slot in the upper portion of the flow meter. The slot has been calibrated to allow the flow rate values to be read during an operation. The blood discharge through the slot must occur in air or oxygen if the flow meter is to function. The amount of air or oxygen trapped in the flow meter is controlled by an air-bleed valve on top of the flow meter. A filter holder is built into the flow-meter assembly. These features allow the flow-meter assembly to serve three useful purposes: flow-rate indication, filtration of the blood, and collection of any air that may enter the system. When the flow meter is used on the delivery side of either pump, a considerable pulse dampening takes place because of the large volume of air or oxygen trapped in it.

Air pressure, vacuum, and electricity are supplied to the pump by rubber hose and electrical cable from the power supply which is located outside of the operating room (Fig. 3). This power source, with the present tubing, can be located 50 feet from the operating table, although with longer tubing, it could be located a greater distance away. The pressure and vacuum are supplied by two air pumps located in this housing. One electrical switch controls the pressure-vacuum pump motors and the motor located on the heart pump.

An explosion-proof motor is located on the heart pump to minimize the danger of an explosion in the operating room. The individual electrical components are all grounded through a common ground lead for safety reasons. Since air pressure and vacuum are supplied by this power source, the heart pump is portable and can be used anywhere that regular 110 volt alternating current is available.

STERILIZATION OF THE ARTIFICAL MECHANISM

Our mechanical heart is so devised that all parts that come in contact with the blood are sterilized by ordinary autoclaving. We believe that this is necessary in order to obtain a high degree of successful experiments. It is significant, we believe, that in our entire group of 65 experiments, not one animal has died of infection.

HEPARINIZATION

During the use of the artificial heart mechanism, blood is rendered incoagulable by using heparin solution. During the early part of our work, we used too small amounts of heparin and occasionally the blood clotted in the pump. On the other hand, when more than 5 mg. of heparin per kilogram of body weight was used some instances of uncontrollable oozing took place. We then began to calculate the amount of heparin to use on the basis of adding the pump volume, which in our case is approximately 300 c.c., to the weight of the

animal. In other words we combine the weight of the animal with the amount of blood contained in the pump. We then put in the citrated blood which is to fill the pump, 1 mg. of heparin per 100 c.c. of citrated blood. The remainder of the calculated dose of heparin is given to the animal. Since we have used this amount of heparin, there have been no instances of clotting in the pump and no instances of uncontrollable hemorrhage.

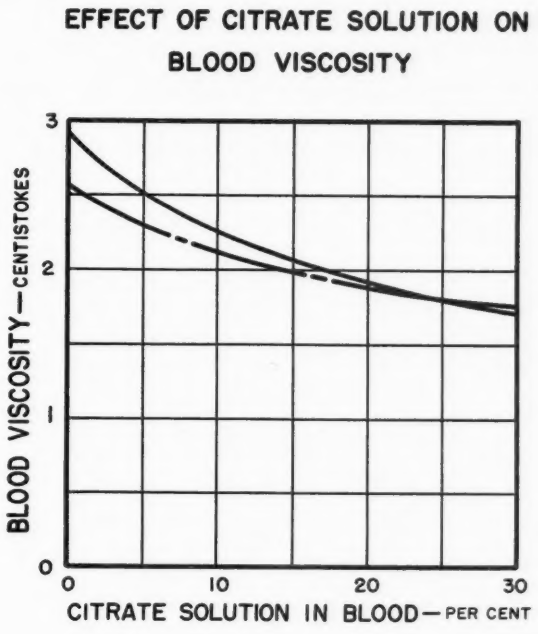


Fig. 4.

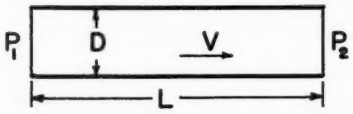
VISCOSITY STUDIES

Since it is necessary to render the blood incoagulable during mechanical pumping of the blood, viscosity studies have been carried out with anticoagulant drugs. Other investigators have found that the heparinization of blood does not affect its viscosity. We have made similar studies using the standard Ostwald Viscosimeter. Our results were the same, namely, that no appreciable change in viscosity takes place with the amount of heparin which is necessary to prevent clotting.

In addition, we have determined viscosity of blood following the administration of large amounts of transfused citrated blood. Since the viscosity of citrated solution is much less than that of blood, it is to be expected that the transfusion of large quantities of citrated blood would affect the viscosity of the circulating blood. Fig. 4 shows a graph of the lowering of the viscosity of blood with given amounts of citrate solution. It is seen from the graph that

a 30 per cent dilution of blood with citrate solution produces a profound lowering of the viscosity. The two lines on the graph represent blood from two different dogs. We have also determined the viscosity of blood from dogs before and after operation of the artificial heart during which time a large amount of citrated blood was transfused. In most of these experiments there has been a profound drop in the viscosity of blood following the procedure. Although the lowering of viscosity is somewhat directly proportional to the dilution, it is not absolutely in direct proportion to it.

POISEUILLE'S EQUATION FOR LAMINAR FLOW



$$P_1 - P_2 = \frac{32UVL}{D^2}$$

$P_1 - P_2$ = Pressure Drop

U = Fluid Viscosity

V = Average Fluid Velocity

L = Length of Pipe

D = Pipe Diameter

Fig. 5.

The viscosity of a fluid passing through a tubular system profoundly affects the pressure necessary to force the fluid through the tubular structure. For rigid tubes this is according to a definite physical law, known as Poiseuille's Law for laminar flow. Although one cannot compare the vascular system to rigid tubes, nevertheless, to some extent, the law may be applicable to the vascular system. Fig. 5 illustrates Poiseuille's Law for laminar flow. Since Poiseuille's Law does not apply for blood in small tubes of less than 0.2 mm. in diameter, it cannot be applied to the arterioles. Bingham and Netting have both modified Poiseuille's Law and these more probably apply to the vascular system.[8] Since the lowering of the viscosity affects the peripheral resistance and, therefore, the force of the pump or heart, we suggest that this may be a factor in some of our animal experiments in which uncontrollable oozing took place.

Since it is a well-known fact that a bleeding diathesis may develop in certain patients who have received large amounts of transfused blood, we suggest that the lowering of the viscosity of the blood of such patients resulting from the great dilution of the blood by the citrate solution may be a factor in uncontrollable oozing. We are not unaware, however, that other chemical changes also take place.

We also wondered if the viscosity of the blood might be changed by the mere mechanical pumping. Viscosity studies were, therefore, carried out on blood which had been drawn from dogs and heparinized. The viscosity was first determined after it was withdrawn and again following thirty minutes of mechanical pumping. We were unable to find any change in the viscosity from the artificial pumping mechanism.

RIGHT-SIDED SUBSTITUTION

Experiments have been carried out in which blood is withdrawn from the right atrium, or vena cavas, passes through the pump and is returned to the pulmonary artery thereby by-passing the right ventricle. We prefer the right atrial appendage to the vena cavas, since with the cannula in the atrium, not only the vena cavas blood is withdrawn but also that from the coronary sinus as well. We have been able to successfully substitute for the right ventricle during periods up to 30 minutes. We have determined, during the course of the substitution, both the pulmonary artery pressure and the aorta pressure.

There are profound reflexes present in the dog with regard to the normal atrial distention. In general this is thought to represent the Bainbridge reflex. Briefly stated, the Bainbridge reflex means that a rise in pressure or increased distention of the great veins or right atrium sends up impulses to the brain center causing an acceleration of the heart rate and, therefore, a rise in the blood pressure. Inversely, the removal of the normal distention of the atrium or great veins should cause a slowing of the heart and drop in blood pressure. In our experimental animals, this reflex, or one similar to it, can be easily produced by mild traction on the right lung. We have noticed this reflex drop in blood pressure constantly with the traction on the right pulmonary artery during its cannulation. Fig. 6*A* shows this profound drop in systemic pressure following traction upon the right lung. The fall in blood pressure begins almost simultaneously with the traction on the lung. Fig. 6*B* also shows a profound drop in systemic pressure as the right sided pump is turned on. It also demonstrates a slowing of the heart rate.

Since it is known that atropine diminishes the nervous impulses taking place by way of the vagi, this drug has been given to determine whether or not this Bainbridge reflex could be abolished. To a large extent, atropine does markedly diminish the lowering of blood pressure due to reflex action. Fig. 6*A* illustrates the fall in blood pressure following traction on the lung and following the administration of atropine. It is seen that the fall is not nearly so great. We believe, therefore, that the use of atropine to diminish vagal reflexes is a sound one. Such a severe hypotensive reflex is obviously not

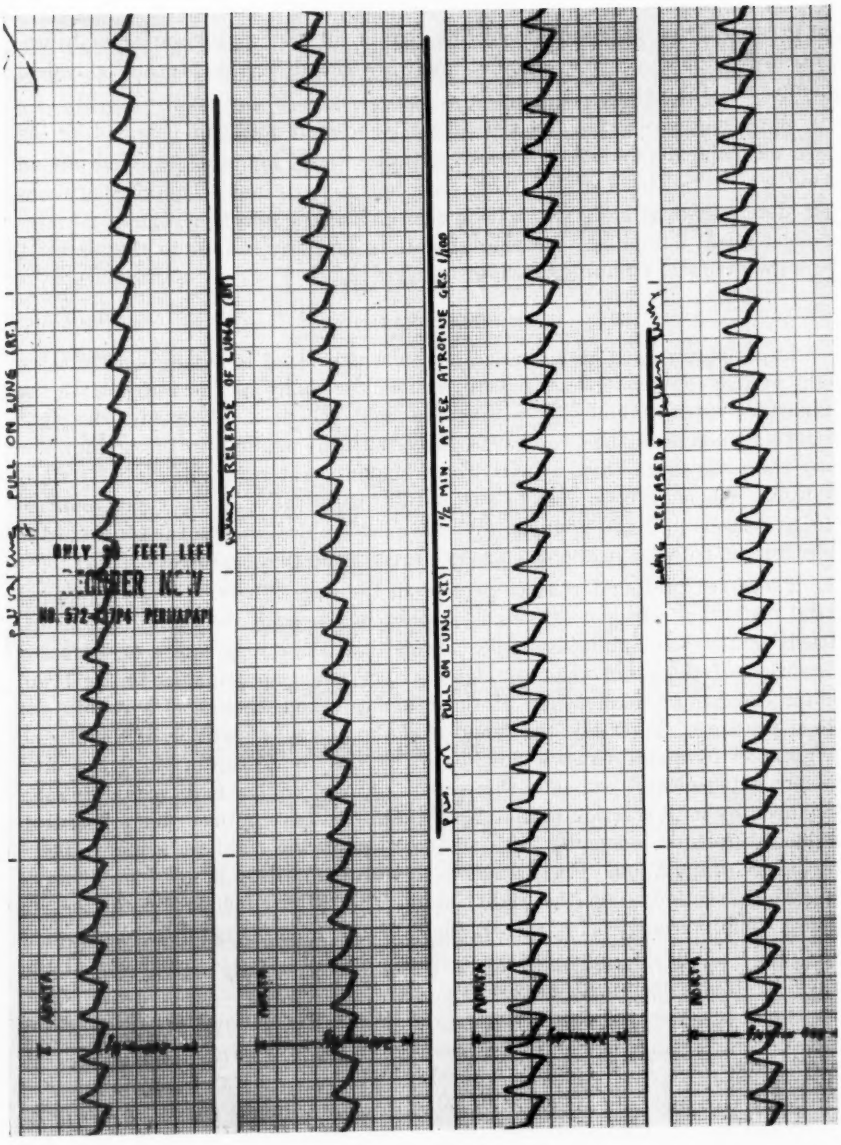


Fig. 64.—Hypotension produced by traction on the right lung. Also shows effect of atropine.

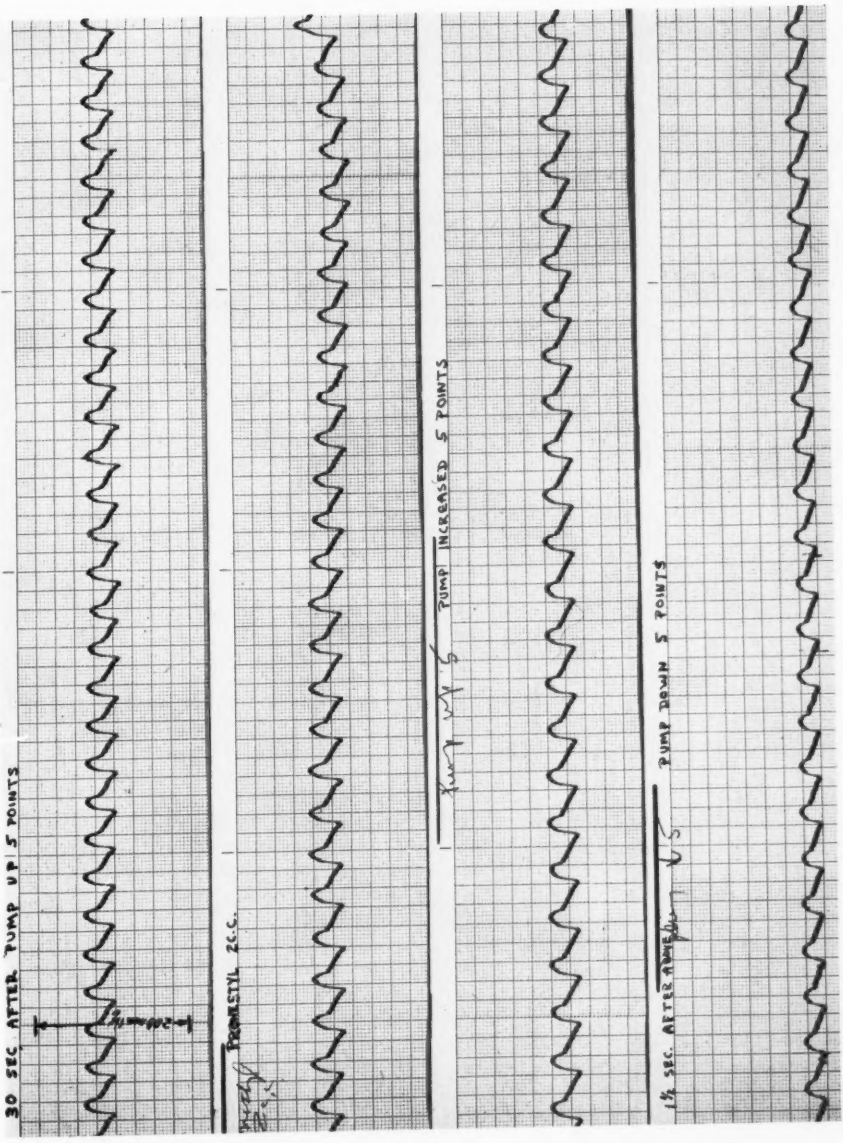


Fig. 6B.—Profound drop in systemic pressure as the right atrium is evacuated; also slowing of the heart.

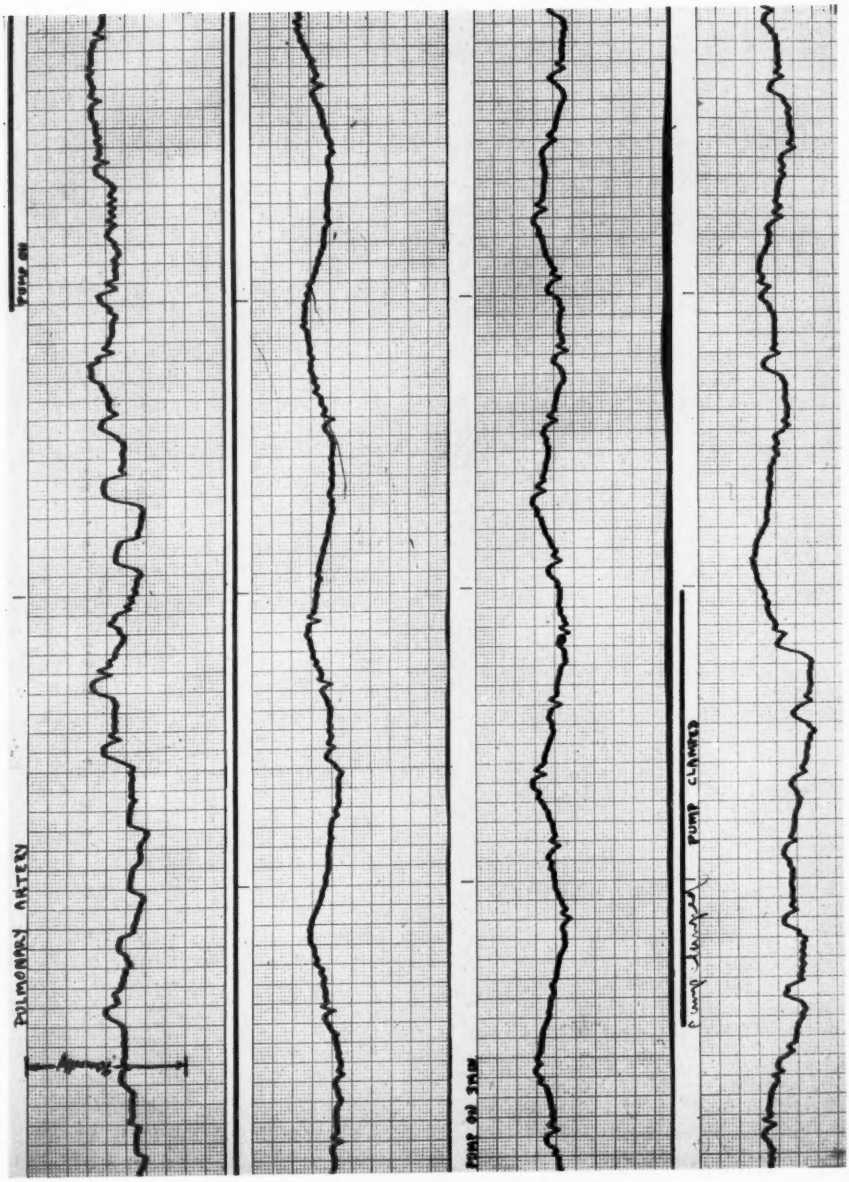


Fig. 7.—Pressure pattern of the pulmonary artery with partial subsitution of the right ventricle.

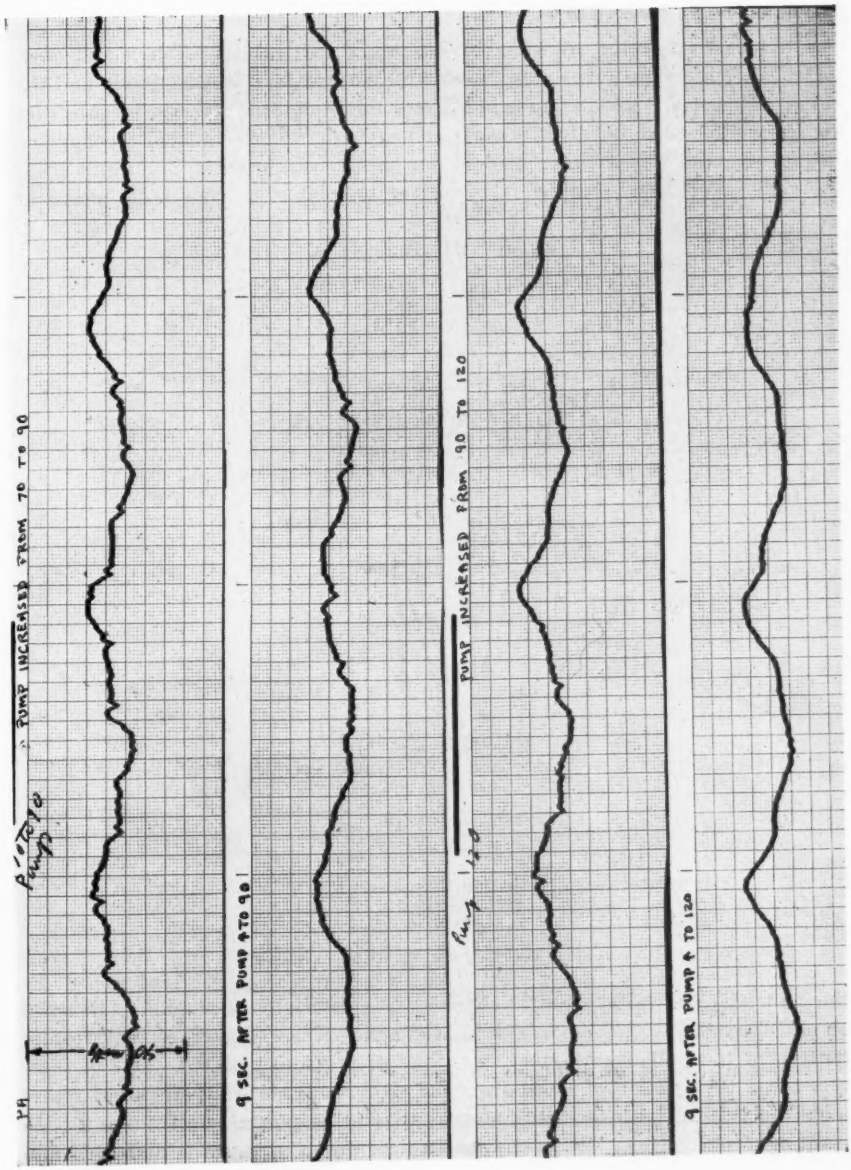


Fig. 8.—Pressure pattern of the pulmonary artery showing complete substitution for the right ventricle. The large waves are due to the respirator.

present in man as it certainly would be observed during right sided lung resections, especially difficult pneumonectomies where considerable traction is placed on the hilar structures.

It has been stated by some investigators particularly Gibbon and associates[1] that the vena cavas must be cannulated proximal to the atrium and the cavas obstructed between the cannula and the atrium in order to be sure that all the right sided blood is being pumped with the mechanical mechanism. We have found that another method may be used in order to determine if all the right sided blood completely by-passes the ventricle. This is by means of

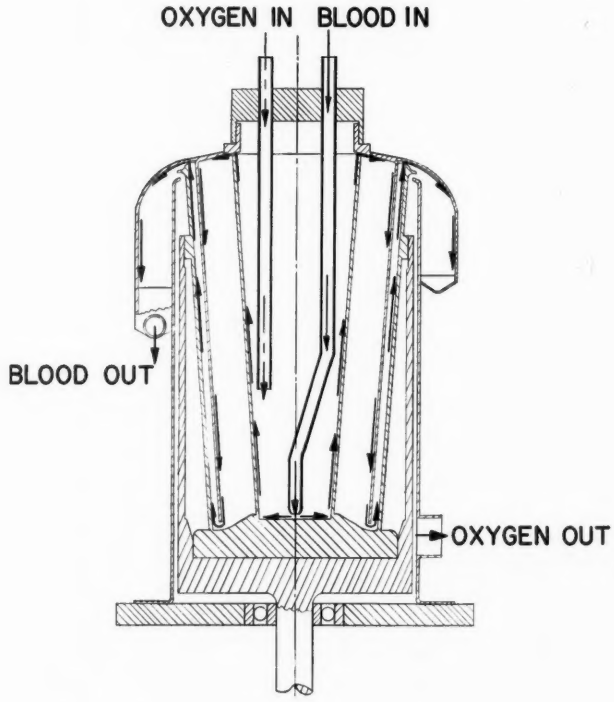


Fig. 9.—Rotating cup oxygenator.

the pulmonary arterial pressure pattern. As the right sided pump is turned on and blood begins to by-pass the right ventricle, there appears in the pressure pattern of the pulmonary artery two types of pressure patterns. One of these represents the ejection of blood from the right ventricle while the other represents the pattern from the mechanical pump during partial substitution for the right ventricle. However, as the mechanical pump pressure is increased and all the blood by-passes the right ventricle, the pressure pattern represented by the ventricular beat disappears and the pattern is then solely from the mechanical pump. Figs. 7 and 8 illustrate partial by-passing of the right

ventricle and later on complete by-passing of the right ventricle. These findings have been confirmed by either aspiration of the right ventricle or by incising it. Later on in this manuscript we shall describe a similar pressure pattern for the left sided circulation.

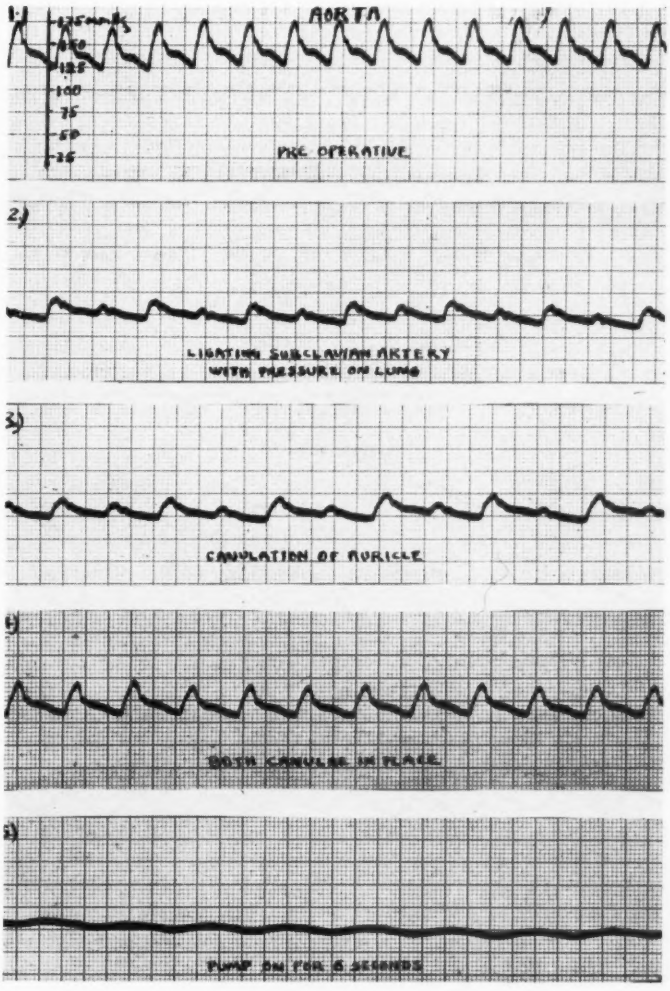


Fig. 10.—Drop in systemic blood pressure with complete extracorporeal circulation.

COMPLETE EXTRACORPOREAL CIRCULATION

An oxygenator which is illustrated in Fig. 9 has been attached to our pump and complete extracorporeal circulation has been carried out. This procedure initiates the same hypotensive reflex as does the right-sided substitution. Fig.

10 illustrates the drop in blood pressure following the evacuation of the right atrium.

In both the right sided substitution and in the complete extracorporeal circulation with mechanical oxygenation, supportive measures to maintain the systemic blood pressure must be initiated if there is to be a high degree of

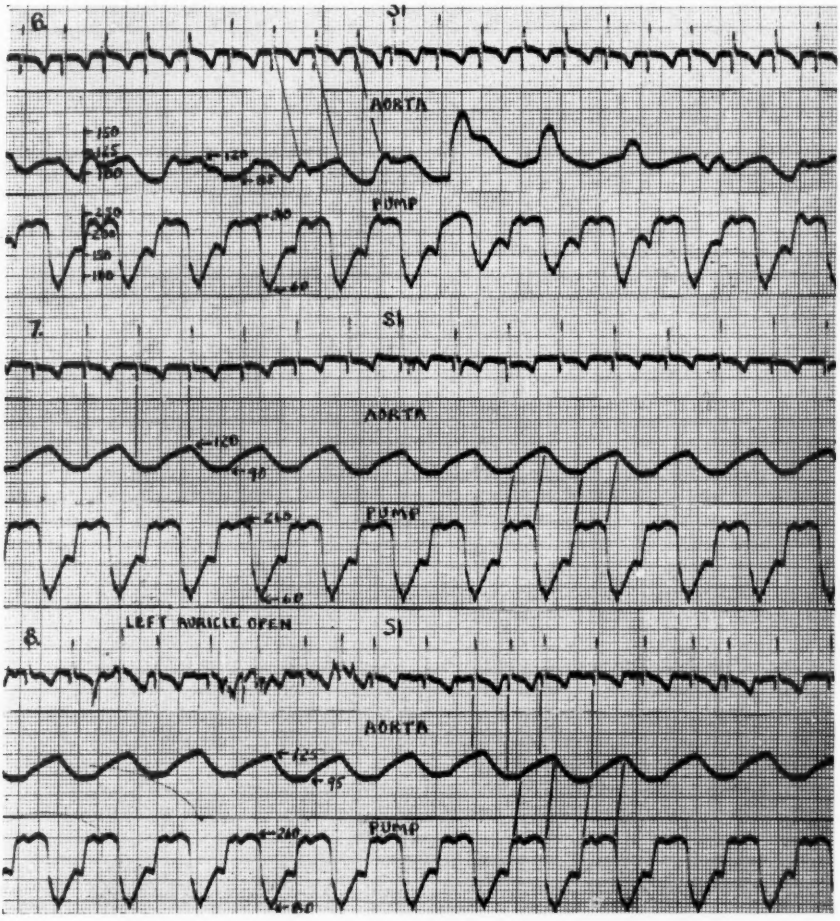


Fig. 11.—Pressure pattern of the aorta illustrating partial and complete substitution for the left ventricle; also, there is no drop in aorta pressure (no Bainbridge reflex initiated).

success with the experiments. In the beginning of our work the great majority of the dogs died until we began to record the continuous arterial pressure. Since then, with the administration of blood and various vasoconstrictor drugs, we have been able to maintain the systemic pressure and our successes are vastly different.

LEFT-SIDED SUBSTITUTION

We have done a large number of experiments in which the left ventricle has been by-passed. This has been accomplished by cannulation of one of the left pulmonary veins, withdrawing the blood into the pump and passing it into the aorta by way of the left subclavian artery. As was previously mentioned, we have found a means of determining when all the blood by-passes the left ventricle. This is by a continuous recording of the aorta pressure patterns. As the pump is turned on, a part of the blood by-passes the left ventricle and there appear two types of pressure patterns in the aorta. These pressure patterns have been obtained, as were those on the right sided experiments, by inserting the Cournand catheter into the femoral artery and up into the aorta. This cannula is connected to Sanborn's multichannel recording apparatus. With this mechanism we have recorded the continuous electrocardiogam, the pressure of the blood in the tubing after it leaves the pump and the pressure patterns in the aorta itself.

With partial by-passing of the left ventricle two types of pressure curves are recorded in the aorta: first, the curve due to the pump; and second, a different type of a curve which represents the ejection of the blood from the left ventricle. This is determined by the simultaneous recording of the electrocardiogram and aorta pressure patterns. As the pump pressure is turned up, however, the ventricular beats are no longer recorded in the arterial pattern and the entire pressure pattern is due to the mechanical pump alone. Fig. 11 illustrates partial by-passing of the left ventricle in which both ventricular beats and artificial pump "beats" are recorded. As the pump pressure is turned up, the mechanical pump takes over the entire left-sided circulation and no ventricular beats appear in the pressure pattern. We have experimented with various ways of walling off the mitral valve from the rest of the atrium containing the suction cannula in one of the pulmonary veins. This has been accomplished by applying a certain type of clamp just proximal to the mitral valve. We have found that, when such a clamp can be properly applied so that no blood gets into the ventricle by way of the mitral valve, the aorta pressure pattern is that from the pump alone and that no ventricular beats appear on the curve of the pressure pattern. We have confirmed this observation on several occasions by opening the base of the left atrium below the clamp which separates the mitral valve from the suction cannula in the atrium and found that there is no blood in the ventricle. By this means, therefore, we can successfully expose the mitral valve for periods of twenty to thirty minutes with survival of the animals.

LEFT-SIDED REFLEXES

We have previously stated that as the right atrium is evacuated of its blood, there promptly develops a severe hypotension which is often fatal unless the blood pressure is supported by transfusion and vasoconstrictor drugs. On the left side of the heart, however, such an atriopressor reflex is not present or, at least, not present to an important degree. Fig. 11 also shows the aorta pressure as the left-sided pump is turned on and as the left ventricle is

completely by-passed. It has been our experience that usually no drop in systemic pressure occurs, although in some experiments we have noted some minor degree of drop in aorta pressure. Atropine will usually abolish the minor hypotensive reflex, if present.

BLOOD CHEMISTRY

During these experiments a large number of tests have been performed on the blood. These have been done before, during, and immediately after the experiments. These include: total protein, sodium, potassium, Ph, Hematocrit, blood counts, oxygen saturation, and chlorides. We shall report these changes subsequently.

SUMMARY

1. Sixty-five experiments on dogs using the artificial heart have been performed. These include: (a) right-sided substitution, (b) complete extracorporeal circulation with mechanical oxygenation, and (c) left-sided substitution.

2. No animals have died of infection. This is due, we believe, to our type of pump which is sterilized by autoclaving.

3. The viscosity of the blood is profoundly lowered following the administration of large quantities of citrated blood.

4. There are profound atriopressor reflexes present on the right side of the heart in dogs which greatly lower the systemic blood pressure, in fact, we have found it necessary to support the blood pressure by large transfusions as well as by the administration of vasoconstrictor drugs.

5. This atriopressor reflex is not present on the left side in dogs or, at least, is not present to the same degree. As a general rule we seldom obtain any drop in systemic blood pressure at all.

6. We present a method of determining when all the blood by-passes the heart. This is by the particular type of arterial pressure pattern obtained.

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DISCUSSION ON "ARTIFICIAL OXYGENATION AND CIRCULATION DURING COMPLETE BY-PASS OF THE HEART," BY DR. JAMES A. HELMSWORTH, DR. LELAND C. CLARK, JR., DR. SAMUEL KAPLAN, DR. ROGER T. SHERMAN, AND DR. THOMAS LARGEN; AND "SOME PHYSIOLOGIC ASPECTS OF THE ARTIFICIAL HEART PROBLEM," BY DR. F. D. DODRILL, DR. EDWARD HILL, AND DR. ROBERT GERISCH

DR. JOHN H. GIBBON, JR., Philadelphia.—I was delighted to hear these two presentations and to learn that other workers are exploring methods of temporarily diverting the blood stream from the heart. I do not feel competent to discuss the physiologic aspects of the second paper, but I have had some experience with the Clark-Golan lung. In our laboratory we were unable to achieve the good results which were reported by Dr. Helmsworth, but I am sure it was because we did not spend enough time developing and perfecting this method. I think a great deal of work must still be done with this apparatus, e.g., developing automatic control of CO_2 tension and pH, before it can be safely used for total by-pass of the heart in human patients.

I would like to show what has been accomplished with the apparatus we have been using—the new apparatus which was completed last summer. The method of oxygenation consists in the passage of blood over stationary vertical screens enclosed in a plastic case. Oxygen is taken up and carbon dioxide given off by the blood while it is filmed on these screens. Thirteen animals have survived experiments in which the entire blood flow was temporarily diverted from the heart and lungs. These operations were performed between August of 1951 and January of 1952. The entire circulation was carried by the mechanical heart lung apparatus; both venae cavae being occluded for periods, with the exception of the first one, of more than an hour, the longest for 100 minutes. All of these dogs are alive and perfectly well months afterward. These thirteen experiments were from a consecutive series of nineteen attempts; two of the nineteen animals died from technical errors and the others died several days following the operations.

(Slide.) This is a graph illustrating the kind of controls we have. In this dog the entire circulation was carried by the heart lung apparatus for ninety-six minutes with the blood pressure maintained in the preoperative range. The blood flow was constantly 1,200 mm. per minute, and the pH was well maintained on the alkaline side by the automatic control of the CO_2 tension in the gas exposed to the blood. The arterial oxygen saturation was well maintained and the venous oxygen saturation also remained at a normal level. The latter we regard as indicative of adequate tissue oxygenation and an adequate blood flow. I think control of the pH of the arterial blood is important as Dr. Helmsworth indicated.

When the heart is opened the disposal of the coronary blood flow is relatively easy to accomplish. The coronary venous return is aspirated from the right atrium and continuously returned to the extracorporeal circuit. When I left Philadelphia we had opened the right atrium in four consecutive dogs, for periods between twenty-five and thirty-five minutes. While the right atrium was open the cardiorespiratory functions were maintained by the extracorporeal blood circuit. These four dogs are all alive and well weeks later.

In conclusion I would like to congratulate Dr. Helmsworth upon the excellent detailed report of the results of his experiments. I believe that we are approaching the time when extracorporeal blood circuits of the mechanical heart lung type can be safely employed in the treatment of human patients.

DR. SANFORD E. LEEDS, San Francisco.—I would like to make just two points, one concerning drainage of the right side of the heart. I would like to illustrate the cannula we have been using for this purpose.

(Slide.) This was published a couple of years ago (*Proc. Soc. Exper. Biol. & Med.* **75:** 468, 1950), but I thought it would be well to bring it up again because drainage of the right side was mentioned. This is a 26-gauge right-angle metal cannula which is passed

into the azygos vein, into the superior cava, down through the right auricle and into the inferior vena cava. It is ligated in place so that blood from both vena cavas must pass out through the cannula and none into the right auricle. We have found this quite satisfactory.

The second point concerns other applications of the mechanical heart. (Slide.) We have recently applied it to occlusion of the thoracic aorta. The carotid artery is cannulated and a plastic tube is passed through the femoral artery and into the thoracic aorta. The blood from the common carotid artery is passed into the reservoir cylinder, through the pump and back into the femoral artery via the plastic tubing. By this means the aorta has been occluded for periods up to three hours, with survival. By applying clamps above and below any place in the thoracic or abdominal aorta, the aorta may be resected and anastomosed. The spinal cord receives an excellent blood supply and we have had no cases of instances of spinal cord damage with this type of surgery. We have encountered a good deal of difficulty with heparin and deheparinization. Some of the anastomoses have bled and the animals have not survived.

DR. JAMES A. HELMSWORTH, Cincinnati.—(Closing.) I want to thank Dr. Gibbon and Dr. Leeds for their contributions to this discussion. To bridge the very large gap between total by-pass of the heart in experimental animals and clinical use of the heart lung machine, many additional studies are required. One simple step to be taken in this evolution of systems to oxygenate and pump the blood is the experimental use of the apparatus for partial by-pass of the heart and lungs in selected patients with disease of the cardiorespiratory system.

We would like to summarize the successful use of the dispersion oxygenator and pump, in a 45-year-old man with extensive fibrotic disease of the lungs and cor pulmonale. His dyspnea, cyanosis, and orthopnea were severe, but the procedure was completed with local anesthesia and without large doses of sedatives. The venous blood was withdrawn through the catheters passed into the inferior vena cava via the saphenous veins; after the blood had been oxygenated and freed of some of its carbon dioxide, it was pumped back into two veins of the right arm. The period of extracorporeal circulation was 75 minutes.

(Slide.) The flow through the extracorporeal circuit was slowly increased until it reached 1280 c.c. per minute. This was equal to approximately one-fourth to one-third of his cardiac output. The blood pressure, which had fallen after the administration of heparin, returned to the normal range. There was an immediate decrease in the rate of respirations and a concomitant relief of dyspnea and orthopnea. The reduction in cyanosis was unequivocal.

(Slide.) The control sample of arterial blood for oxygen saturation was unsatisfactory. In the pumping period the range of saturation was 55 to 60 per cent. After the period of dispersion oxygenation, the arterial oxygen saturation fell into the range of 40 per cent, the control level for this patient's state of cardiorespiratory dysfunction. The plasma carbon dioxide tension fell and the carbon dioxide content and pH rose. There was an increase in the leukocyte count. The erythrocyte count was unchanged and the concentration of hemoglobin remained exactly the same. The quantity of hemoglobin in the supernatant plasma was too small to be determined accurately by routine methods.

The patient experienced definite relief of symptoms during the 75 minutes of partial by-pass. He was given antibiotics for several days and left the hospital without obvious change in the course of pulmonary fibrosis and cor pulmonale.

DR. DODRILL.—(Closing.) I should like to show a 2-minute movie illustrating the exposure of the mitral valve. This was accomplished because we were able to record this particular type of pressure pattern in the aorta and to know that the left ventricle was completely by-passed.

(Movie.) This is a by-pass of the left ventricle. A suction cannula is in the left atrium, having been placed into it by way of the superior pulmonary vein, and the outflow from the pump is into the aorta by way of the left subclavian artery. A clamp has been placed at the base of the left atrium which is between the suction cannula and the mitral valve. In a moment you will see the mitral valve and, through it, into the ventricle which you see does not contain blood. If we open the base of the atrium when there are still ventricular beats in the pressure pattern, there will be not only a great hemorrhage but also air will be sucked into the pump and death of the animal will quickly occur. We can see some motion of the mitral valve but this is in direct relation to the heartbeat itself and we have not been able to demonstrate independent motion of the valve itself.

TECHNIQUE OF PRODUCING MITRAL STENOSIS OF CONTROLLED DEGREE

ROBERT G. ELLISON, M.D., ROBERT C. MAJOR, M.D., RAYMOND W. PICKERING, M.S. (BY INVITATION), AND WM. F. HAMILTON, PH.D. (BY INVITATION)
AUGUSTA, GA.

A PRACTICAL technique of creating mitral stenosis for experimental study has long been considered necessary for better understanding of the disease as it occurs clinically. In 1902 Sir Lauder Brunton[1] suggested the feasibility of surgical correction of this crippling disease, emphasizing that such a procedure depended upon mastering of certain technical details. The development of these skillful surgical techniques could only be accomplished in the experimental laboratory. During the following years, many important contributions were made by Bernheim,[2] Allen,[3] Cutler,[4] Wilson,[5] Powers,[6] Katz,[7] Shaw,[8] and Connolly[9] in their attempts to produce mitral stenosis experimentally. Although the results were in general unsatisfactory, significant observations were recorded. Diverse methods to produce a narrowing of the mitral orifice were devised and used with varying degrees of success. These included placement of sutures across the mitral orifice either above or below the coronary vessels, transplantation of pericardium or fascia across the valve orifice, and traumatization to the valve leaflets with simultaneous inoculation with virulent cultures of streptococcus viridans. Connolly recently reported encouraging results. He placed sutures below the coronary vessels in such a manner that they encircled the chordae tendinae so that during systole the valve leaflets closed without regurgitation but during diastole the suture was sufficiently tight to produce a stenosis. Many of these animals died within a few days from acute pulmonary edema but he thought that a significant number survived for a reasonable period of study.

Now that the stenosed valve can be successfully attacked surgically (Harkin[10] and Bailey[11]), it is of even greater importance that the disturbed dynamics in the disease be better understood. The mechanism of pulmonary edema, once thought to be simply on the basis of back pressure, needs further clarification. Analysis of the factors which produce an increase in the pulmonary bed resistance is greatly needed. These problems can be studied only in the experimental animal with chronic mitral stenosis and back pressure existing over a period of many months or years. The present study is an attempt to produce such an experimental animal.

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Read at the Thirty-second Annual Meeting of The American Association for Thoracic Surgery, Dallas, Texas, May 8-10, 1952.

METHODS

The early attempts involved the passage of a small ureteral catheter around the base of the mitral valve. This was accomplished by inserting the catheter beneath the epicardium just above the coronary vessels, gently advancing it until it encircled the valve. A heavy silk suture, tied to the end of the catheter, was then threaded around the base of the valve as the catheter was withdrawn. Later a flexible probe which could be manipulated more easily was substituted for the catheter. A smooth stenosis at the base of the mitral valve (Fig. 1) was thus accomplished, but serious hemorrhage occurred in approximately 50 per cent of the cases. In order to minimize bleeding and simplify surgery, a long, straight, round needle threaded with silk or nylon, was inserted through the heart from the posterior aspect, passing just to the right of the interatrial groove and just above the interventricular groove. Each end of the suture was anchored

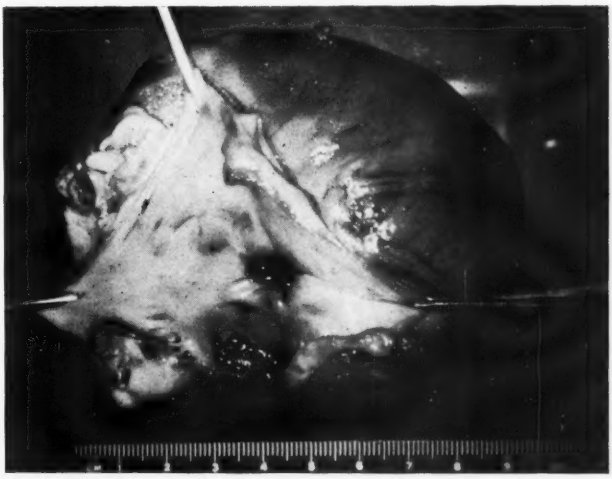


Fig. 1.—Mitral stenosis produced by advancing ureteral catheter around base of valve; pulmonary edema and death on third postoperative day.

anteriorly in the epicardium just above the coronary vessels. Ligatures so placed were tied tightly enough to distend slightly the left auricular appendage. It was impossible to determine the proper degree of stenosis, however, and the dogs either died within a few hours to a few days from pulmonary edema or remained clinically well indefinitely. Autopsy of the dogs revealed a smooth stenosis at the base of the valve with little or no distortion of the leaflets.

The technique was then modified in several respects and the following method is now used: The animals are premedicated with morphine, using the dosage of 10 mg. per kilogram of body weight, and anesthetized with Nembutal, 20 mg. per kilogram. An endotracheal catheter is placed and positive pressure respiration carried out by means of a respirator. The left pleural cavity is entered through the fifth intercostal space. The pericardium is opened widely

just anterior to the phrenic nerve and held open by means of traction sutures. Another traction suture of fine silk is placed in the apex of the heart. The index finger of the left hand is placed between the pulmonary artery and the left auricular appendage and then advanced posteriorly until it indents the medial wall of the right atrium. As the heart is displaced out of its pericardial bed, the left thumb indents the lateral wall of the right atrium so that the index finger and thumb approximate the atrial walls. A No. 20 gauge needle, into the end of which a steel wire has been previously anchored and threaded into nylon tubing, is then inserted through the walls of the right atrium passing just to the right of the interatrial groove and just above the A-V groove and

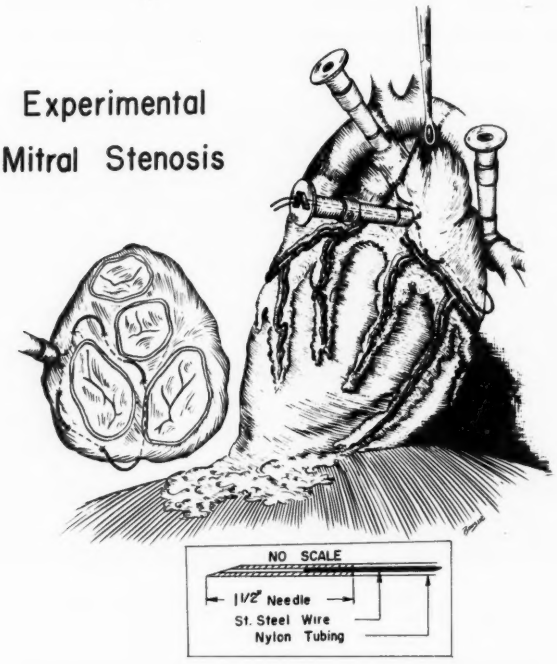
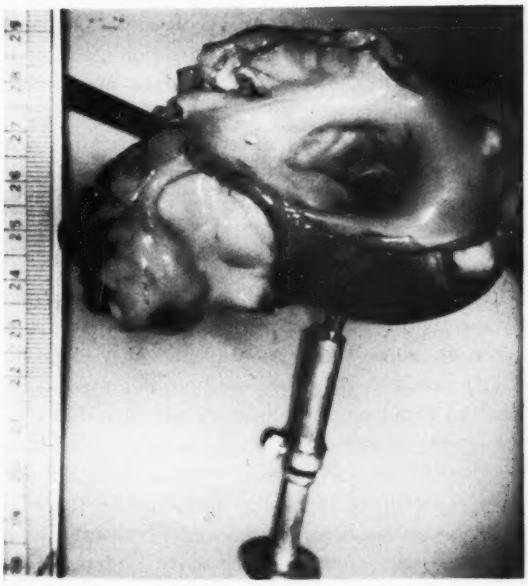


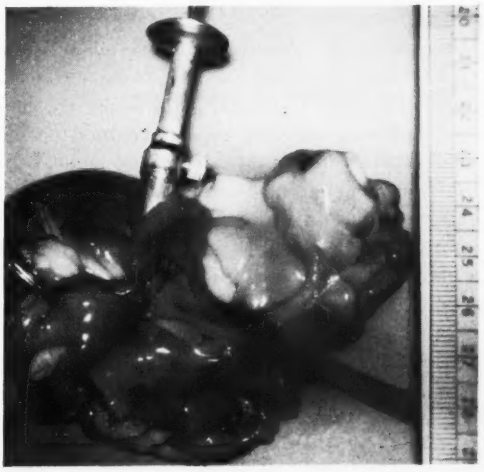
Fig. 2.—Drawing illustrating relationship of suture to base of auricular appendage and coronary vessels. Inset at left indicates passage of suture through right atrium. Lower insert illustrates needle.

emerging anteriorly at a similar position. Each end of this suture has been previously prepared with a needle and is anchored in the epicardium just above the coronary vessels. The suture thus occupies a position at the base of the mitral valve (Fig. 2). Controlled narrowing of the mitral orifice was produced as follows: Instead of tying the suture as had been done in the past, it is passed through a cannula whose large, flat head is affixed to the chest wall subcutaneously and whose cardiac end prevents displacement of the heart as the ligature is tightened at a later date (Fig. 3, *A* and *B*). The animals tolerate

this operative procedure well. No difficulties were encountered from the standpoint of fibrillation and seldom was there significant bleeding. Occasionally bleeding occurred at the site of passage of the suture into the wall of the right



A.



B.

Fig. 3.—*A*, Suture has been placed loosely around base of valve and threaded into cannula. *B*, the size of the mitral orifice is reduced by tightening the suture.

atrium posterolaterally and in these cases hemostasis was easily accomplished by a figure of eight suture of Deknatel No. 5-0. In the earlier cases, angiostomy cannulas, which have previously been described (Hamilton[12]), were placed upon the pulmonary artery and the pulmonary vein so that the pressures could be recorded simply by the insertion of long needles into the vessels through the cannulae. Because of the high incidence of infection associated with this large quantity of foreign material, the use of the angiostomy cannulae has recently been abandoned and pressures obtained by means of cardiac catheterization. After the animals have fully recovered from the operative procedure, usually fourteen to twenty-one days, they are premedicated and anesthetized in the same manner. A 1 cm. incision is made directly over the head of the cannula, the wire suture exposed and tightened, the suture being maintained in that position by means of a silver clip.

In some of the earlier cases the pulmonary capillary pressure was used as a guide to determine the proper degree of tightening. It was discovered, however, that if the mitral orifice was narrowed sufficiently to produce a significant elevation in capillary pressure, the dogs would not tolerate this degree of narrowing and would proceed rapidly into pulmonary edema and death. Consequently, more recently the degree of narrowing has been determined by palpation of the femoral arterial pulse and the wires tightened until there is a perceptible change in volume or rate. The suture is usually shortened in the range of 1 cm. the first time. A smooth stenosis is thus produced at the base of the mitral valve causing no interference with closure of the valve leaflets. The operative mortality is minimal and the suture has been accurately placed in 95 per cent of the cases.

RESULTS

By means of this technique chronic mitral stenosis has been produced in ten dogs that have survived two and one-half to seven months. In one case the suture was improperly placed and partially occluded the tricuspid orifice. All but one of the remaining nine animals developed chronic heart failure. Some were autopsied at varying lengths of time, some were allowed to go downhill and to die from heart failure after a period of observation of several months, and others were maintained in a state of chronic heart failure by loosening or tightening the suture when necessary. By this means the stenosis could be controlled and the animals maintained in a state of chronic failure indefinitely. No attempt, however, has been made at this time to maintain a dog longer than seven months. It was found that if the mitral orifice is narrowed suddenly to within the range of 1 cm. in diameter, the dogs develop pulmonary edema and usually die within a few days. On the other hand, if the orifice is narrowed gradually over a period of several weeks, the dogs easily tolerate a stenosis of 1 cm. in diameter without any difficulty. It is estimated that a mitral orifice of 5 to 8 mm. in diameter, produced by gradually narrowing the orifice over a period of several months by shortening the wire suture on two or preferably three occasions, will maintain a dog in a state of chronic failure.

These dogs develop ascites and edema of the lower extremities at varying periods after tightening. In some cases the onset of failure develops within a week and, if it seems to be progressing rapidly, then the suture is loosened slightly. It has been necessary for numerous paracenteses to be done, five or

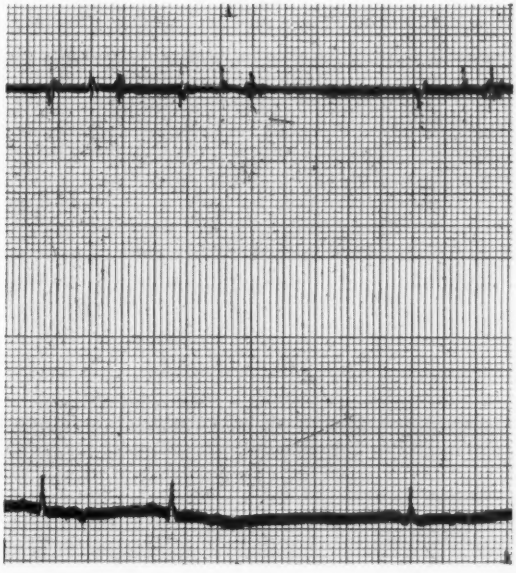


Fig. 4.—Phonocardiogram of Dog No. 75 showing murmur in early diastole, six weeks after tightening of suture.

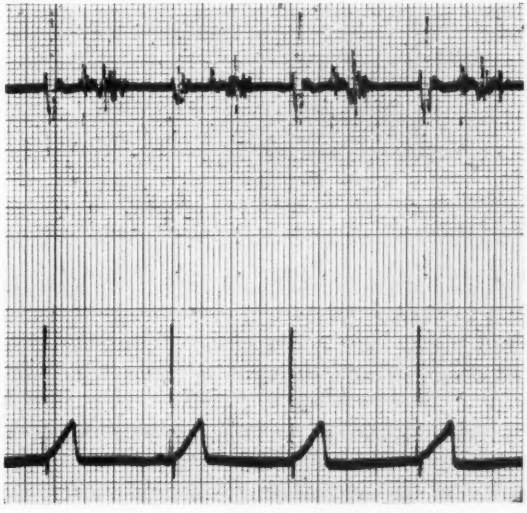
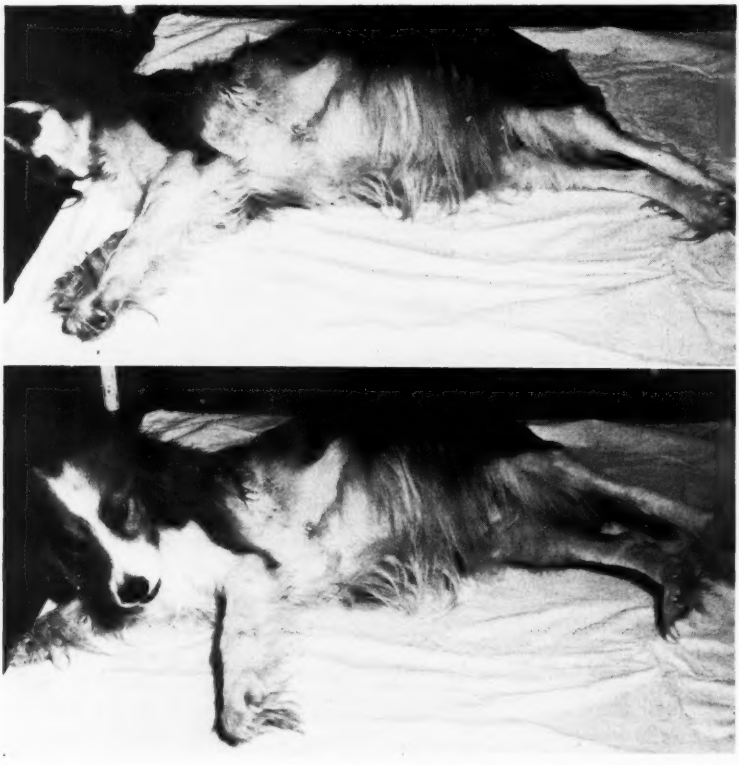


Fig. 5.—Phonocardigram of Dog No. 76 showing diastolic murmur, two weeks after tightening.

six liters of fluid being removed frequently. The dogs have tolerated this state of chronic failure remarkably well. The marked ascites seemed out of proportion to the limitation of activity. In one case ascites developed one week after the first tightening and cleared spontaneously, only to recur several weeks later and persist.

A.



B.

Fig. 6.—Photographs of Dog No. 59. The abdomen is markedly distended with fluid and the lower extremities are edematous five months after tightening of suture.

In all cases a diastolic murmur has been audible. In most cases the murmur could be picked up by phonocardiography (Figs. 4 and 5), but occasionally the murmur was so soft that it could not be recorded. It is noted that the murmur is usually in early or mid-diastole but never in a presystolic position as is heard clinically.

In regard to the dynamics of the pulmonary circulation, it was observed that in all cases the degree of heart failure seemed out of proportion to the amount of elevation in the capillary and pulmonary artery pressures. Also, none of the dogs developed significant elevation in jugular venous pressure,

thus suggesting the possibility of some mechanism other than back pressure to produce the picture of heart failure. Dog No. 59 survived for a period of seven months in a state of chronic heart failure with massive ascites and edema of the lower extremities (Fig. 6, *A* and *B*). Pulmonary artery pressures in this case were recorded by means of a needle inserted into a cannula previously placed on the pulmonary artery. During this period of time the highest recorded pulmonary artery pressure was 40/20 mm. Hg., and right ventricular pressure was 40/0 mm. Hg. The day before death this dog had a massive hemoptysis,

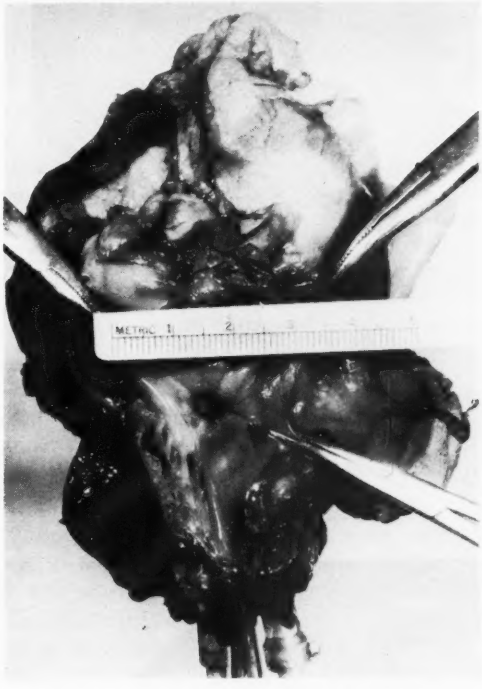


Fig. 7.—Photograph of mitral valve from the auricular aspect (Dog No. 66). Stenosis present for four and one half months. Note smoothness of stenosis and rim of fibrosis on proximal margin.

amounting to approximately 250 c.c. of fresh blood. On the day of death catheterization revealed a capillary pressure of 15 mm. Hg. At autopsy the mitral orifice was found to be 7 mm. in diameter and adjacent to the suture a fibrous ring was forming on the endocardial surface. The valve leaflets were uninvolved and when water was injected under pressure into the left ventricle, the valve leaflets closed without evidence of regurgitation. The right ventricular wall was increased to about twice its usual thickness. The dog died in acute pulmonary edema so that the right ventricle and right auricle were markedly distended and all viscera were markedly congested.

Fig. 8, *A*.

Fig. 8, *B*.

Fig. 8.—Photographs of Dog No. 74 showing distention of abdomen with fluid.

Dog No. 66 was killed accidentally at the end of four and one-half months after narrowing of his mitral orifice. No evidence of ascites developed in this dog but he had a pulmonary artery pressure of 30/10 mm. Hg. with a capillary pressure of 10 mm. Hg and right ventricular pressure of 30/0 mm. Hg. At autopsy the mitral orifice was approximately 4 mm. and it is observed here too that a ring of fibrous tissue developed opposite the suture on the endocardial surface (Fig. 7).

Dog No. 74 developed evidence of acute congestive failure on the second day after his mitral orifice was narrowed. The suture was loosened and he seemed to recover from his heart failure but three weeks later began to develop ascites and edema. At this time catheterization revealed a capillary pressure of 10 mm. Hg, pulmonary artery pressure of 30/12 mm. Hg, and right ventricular pressure of 30/0 mm. Hg. Four liters of ascitic fluid have been removed on three occasions. This dog has a soft, mid-diastolic murmur. He has been in a state of chronic failure for three and one-half months and, in spite of the markedly distended abdomen, is active at the present time (Fig. 8*A* and *B*). Recent catheterization revealed no significant change in pressures.

Dog No. 75 developed ascites one month after narrowing of the mitral orifice. Three liters of fluid have been removed twice and two and one-half months after narrowing of this valve he has a pulmonary capillary pressure of 15 mm. Hg, pulmonary artery pressure of 40/16 mm. Hg., and right ventricular pressure of 40/4 mm. Hg.

Dog No. 76 was tightened on two occasions and three weeks after the second tightening he developed evidence of ascitic fluid. He then went progressively downhill and when it seemed as if he were dying in chronic failure, the wire was loosened slightly. This was followed by marked improvement in his general condition and since then he has been active with a markedly distended abdomen. Catheterization at three and one-half months after the initial tightening revealed capillary pressure of 15 mm. Hg, a pulmonary artery pressure of 33/15 mm. Hg and right ventricular pressures of 30/0 mm. Hg.

All cases were studied by electrocardiography. In one case (No. 59) there was electrocardiographic evidence of right ventricular strain (ischemic changes) which persisted to the time of death of the animal.

The complications of this technique have been minimal. In one case a thrombus of fairly large size developed around the suture in its course through the right atrium so that the tricuspid orifice was partially occluded.

DISCUSSION

Further study is necessary in order to adequately evaluate problems that have arisen in connection with this technique. Although no evidence of coronary damage has been detected to date, eventually evidence of myocardial ischemia may be noted in the electrocardiogram. These dogs need to be maintained in a state of chronic failure over a much longer period of time in order to adequately evaluate the effect of elevated back pressure on the pulmonary circulation. Additional study is necessary also to further clarify the early development of failure in the presence of minimal elevation of back pressure.

SUMMARY

A technique of producing chronic mitral stenosis of controlled degree in the experimental animal has been described. This technique has satisfactorily produced the picture of chronic mitral stenosis simulating the clinical picture of this disease in man. Further studies are necessary in order to elucidate some of the observations recorded.

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DISCUSSION

DR. OTTO C. BRANTIGAN, Baltimore.—Dr. Sim Penton and I have worked on the problem of producing mitral stenosis. After trying many methods without success it was found that rubbing ground glass in No. 2 plain catgut suture would produce stenosis if the suture were passed through the valve leaflets. The valves became contracted and scarred with definite excrescences and there was definite narrowing of the valve orifice.

DR. ELLISON.—(Closing.) I would like to thank Dr. Brantigan for his comments. Some of the problems that have arisen in connection with this technique still have to be clarified. Whether or not this rim of fibrosis that is developing at the site of the stenosis will interfere with later control of the stenosis we do not know. Since the fibrosis may not develop until four to six months after the valve has been narrowed, it may be that the animals will be compensated by that time and will be in a state of chronic failure, so that further control of the stenosis will be unnecessary.

SURGICAL APPROACH FOR STENOTIC LESIONS OF THE SEMILUNAR VALVES BY EXCISION AND CUSP REPLACEMENT UNDER DIRECT VISION

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BOSTON, MASS.

STENOTIC lesions of the pulmonary and aortic valves possess certain intrinsic anatomic, pathologic, and physiologic similarities.

From the standpoint of construction, both are semilunar valves and both completely depend upon their lateral attachments to the vessel wall for support.

Pathologically, both lesions present the familiar picture of thickening, commissural fusion and fixation of the semilunar cusps with a small central ostium. The valve in most cases of pulmonary valvular stenosis, although firmly fixed, is inclined to be a thin, domelike structure. In older patients, however, a thicker and more rigid valvular structure is sometimes seen.

In rheumatic aortic stenosis, the inflammatory process produces conglutination of the adjacent cusps at the commissures as well as thickening of the cusps themselves. With organization and scarification, the cusps become rigidly fixed and fused. Often, retraction and severe deformity of the cusps result in associated aortic regurgitation.

Thus, the primary physiologic problem in both cases is an obstruction of ventricular ejection. Experimental data[1] and clinical observations indicate that little alteration of the circulatory dynamics occurs until the outflow tract is reduced to approximately one-fourth its normal size.

This is readily explained by an analysis of the factors involved in the expending of the mechanical energy of the heart. By far the greatest single factor in myocardial work is the energy required to eject a definite volume of blood from the ventricular chambers against a peripheral resistance. A second factor is the energy required to impart velocity to the blood stream.

Ordinarily, calculations of myocardial work neglect the velocity factor since it is assumed that it constitutes but a very small part of the total work of the heart. Normally it amounts to only 1 or 2 per cent. However, in the presence of a stenotic lesion, interference with the ability of the ventricle to

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impart velocity to the blood results in an increase in the velocity factor so that it may rise upward to the magnitude of 50 per cent of the total work of the heart.[2]

Until there is marked obstruction of the valvular orifice (approximately 75 per cent), increased velocity flow readily compensates for the stenotic lesion with only a small increase in cardiac work. With more marked obstruction, maintenance of cardiac output by increased velocity flow results in a marked expenditure of myocardial energy, a situation which eventually results in cardiac failure.

Fig. 1, adapted from Evans,[2] graphically illustrates the effect of semilunar stenotic lesions on myocardial work. The velocity factor, at first negligible, rapidly outstrips the resistance factor.

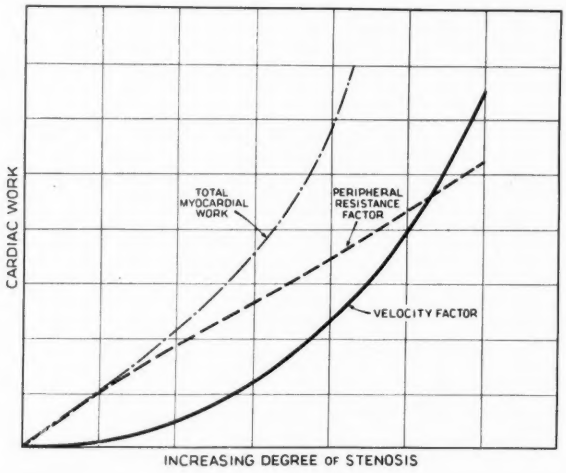


Fig. 1.—Curves showing the effect of increasing degrees of stenosis on the velocity factor of myocardial work.

Thus, what is required is a return to a higher efficiency area seen below the critical point of obstruction (approximately 75 per cent). With this accomplished, the circulatory dynamics will have returned to a point at which the velocity factor is again small so that the total myocardial work will be markedly diminished.

Because of the basic similarity of pulmonary and aortic valvular stenosis, any consideration of surgical therapy for one lesion would correspondingly suggest a method of approach for the other. This, indeed, has been the case. The purpose of this communication is to present an approach which is believed to surmount the pathophysiologic problems associated with both lesions.

The technique consists of resection of a pulmonary or aortic cusp and valvular reconstitution by organic cusp prostheses and homograft cusps.

An important factor in these procedures has been the design of instruments which permit resection of one-third of either the pulmonary or the aortic valve (one cusp) under direct vision. Interruption of the circulation is not necessary.

PULMONARY VALVULAR STENOSIS

The first attempt to treat pulmonary valvular stenosis was made by Doyen in 1913.[3] He attempted to cut the valve by insertion of a tenotomy knife into the right ventricle. The patient survived the procedure but died a few hours postoperatively. Necropsy demonstrated a subvalvular rather than a valvular stenosis.

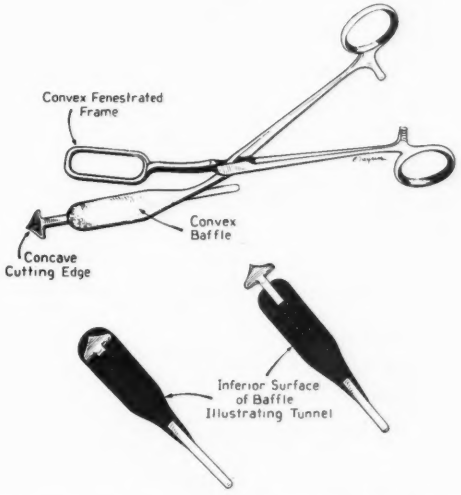
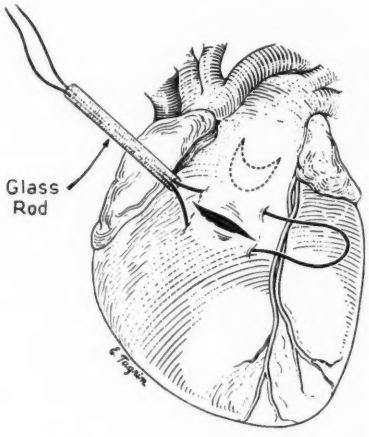


Fig. 2.—Instrument used for pulmonary cusp resection and replacement.

Following this, there was a hiatus of over 30 years until the entire field of congenital heart disease was reopened by the monumental report of Blalock and Taussig[4] in 1945. The ingenious aortic-pulmonary arterial shunt of Potts, Smith, and Gibson[5] soon followed. Finally, in 1948, Sellors[6] and Brock[7] both reported successful direct attacks on the stenotic pulmonary valve by valvulotomy. Recently, experimental[8] and clinical attempts[9] have been made to carry out pulmonary valvulotomy under direct vision by means of temporary occlusion of the circulation.

It is clear that surgery done under direct vision is far superior to that done blindly. Equally desirable is an uninterrupted circulation. It has been possible to attack the pulmonary valve with an instrument which accomplishes both of these requisites (Fig. 2). It consists essentially of three parts. The first is a convex solid baffle. Situated above this is a convex fenestrated frame which tightly rims the baffle when the clamp is locked. The third component is a con-

cave cutting edge which directly underlies the baffle in a tunnel, as illustrated. Advance of the cutting edge is limited to a distance of one-half inch. When not in use, a spring mechanism (not shown) retains the cutting edge under the baffle.



TECHNIC OF PURSESTRING SUTURE

Fig. 3.—For description, see text.

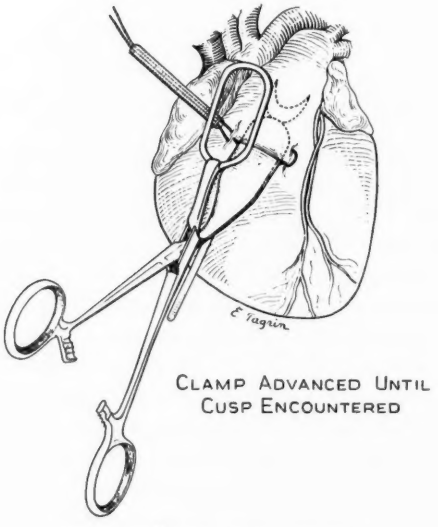


Fig. 4.—For description, see text.

METHOD

Mongrel dogs were used, varying in weight from 7 to 15 kilograms. Intravenous pentobarbital sodium was used to obtain anesthesia. Intermittent positive pressure insufflation was administered through an endotracheal tube.

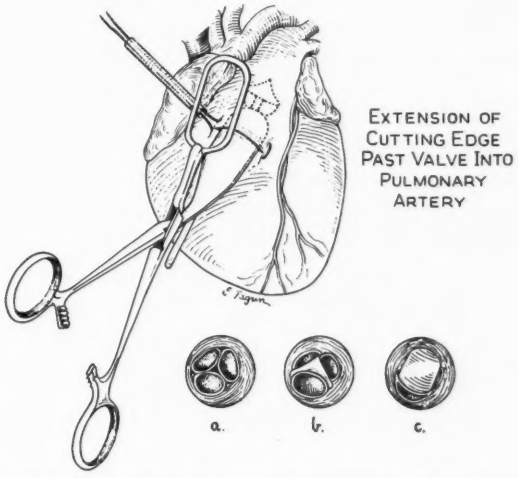


Fig. 5.—*a*, Pulmonary valve viewed from pulmonary arterial side, *b*, concave cutting edge extended past valve, *c*, convex baffle advanced past valve.

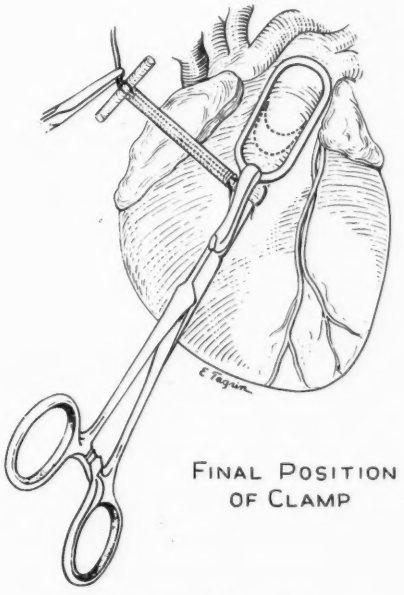


Fig. 6.—For description, see text.

The chest was entered through the left fourth intercostal space and the pericardium overlying the right ventricle was opened widely. Marsupializing the free edges of the pericardium improved the exposure. A purse-string type of suture of 0 braided silk was then placed approximately 1.5 cm. from the valve ring (Fig. 3). Both free ends were fed through a small glass tube. We have found that this method permits instantaneous hemostatic control and eliminates the necessity of having two assistants cross stay sutures, with the confusion and blood loss coincident to this maneuver. Sharp-pointed Adson scissors were gently pushed through the myocardium between the purse-string suture and an incision approximately 1.5 cm. long was made. The baffle and its underriding semilunar cutting edge, having previously been moistened with heparin, was quickly introduced into the ventricle and the purse-string suture tightened. The baffle was then advanced until the approximate level of the anterior cusp of the pulmonary valve was reached (Fig. 4). At that point, the concave cutting edge was extended past the valve into the pulmonary artery and then retracted

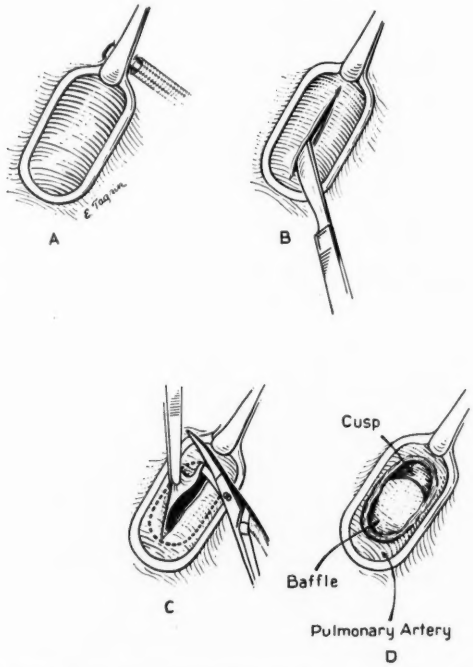


Fig. 7.—Technique of excision of pulmonary cusp prior to replacement with homograft cusp. Illustrations drawn from pulmonary arterial aspect.

under the baffle which, in turn, was advanced past the valve. In Fig. 5, *a*, *b*, and *c* illustrate these steps as viewed from the pulmonary arterial aspect. Naturally, in the absence of a valvular stenosis in the dog, the use of the concave cutting edge was quite unnecessary. Its chief value, however, lies in the familiarization of the operator with conditions as they will be seen in the human being. Fig. 6 illustrates the final position of the instrument. The purse-string suture was tightened and secured by means of a transverse glass rod and hemostat, as shown. With the clamp locked, the anterior pulmonary cusp and its overlying pulmonary arterial wall were effectively interposed between the underlying baffle and overlying fenestrated frame. Thus, the baffle created an artificial wall in the conus area which permitted excision of

the cusp under direct vision. By virtue of its convex shape, it closely conforms to the luminal curve of the conus so that the outflow tract is unobstructed with the instrument in situ.

The precise technique of cusp excision varied with the two basic methods of cusp replacement employed.

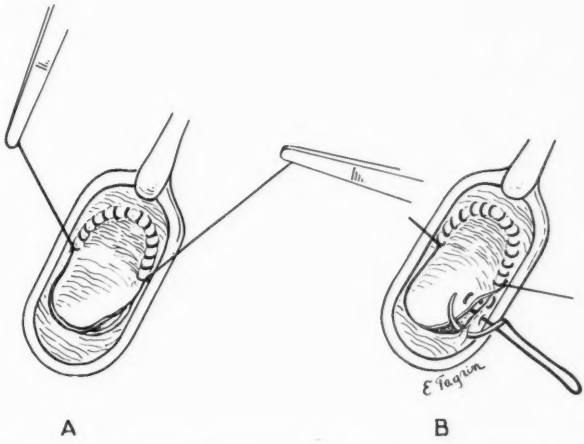


Fig. 8.—Technique of suturing homograft in place. Two stay sutures have been placed at the superior commissural points of the donor and lateral cusps to insure accurate positioning.

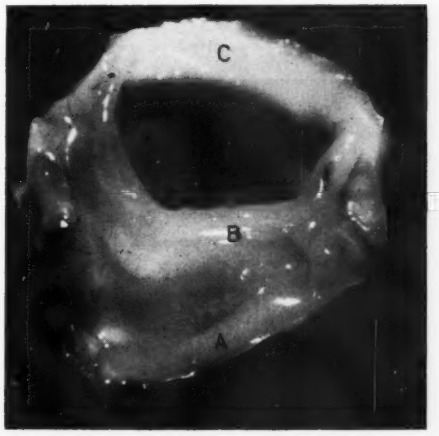


Fig. 9.—Trimmed aortic cusp homograft. *A*, Annulus, *B*, cusp, *C*, aortic wall.

The first method of pulmonary cusp replacement was the use of pulmonary or aortic cusp homografts. These were obtained from donor animals and consisted of either a pulmonary arterial or aortic segment and an attached cusp.

Fig. 7 illustrates the technique of cusp excision when a homograft cusp was to be inserted. A vertical incision was made over the baffle and the cusp visualized. With the cusp satisfactorily in view, an elliptical segment of pulmonary arterial and right ventricular wall was excised and, finally, the cusp. The homograft cusp was then sutured in place (Fig. 8).

An important point in the accurate positioning of the homograft cusp was the placing of two stay sutures on each side of the donor cusp at its most superior point. By visualizing the superior commissural points of the lateral cusps of the recipient and placing sutures at those points, the graft was placed in exactly the proper position. It is imperative that the superior or lunular edges of the cusps meet exactly. If they do not accurately coapt, regurgitation will be the inevitable result. Failure to carry out this technical point initially resulted in faulty placement and subsequent diastolic murmurs in a number of our animals.

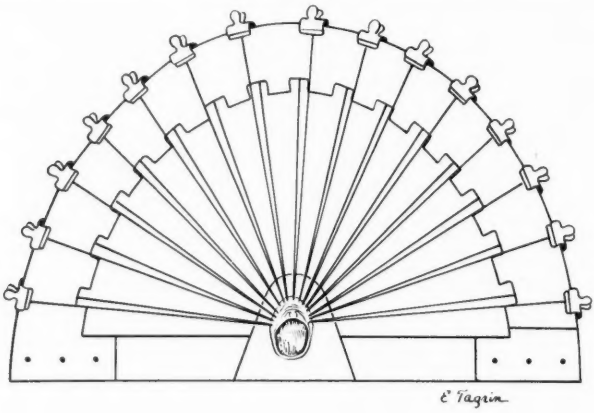


Fig. 10.—For description, see text.

Fig. 11.—Trimmed pulmonary cusp homograft (retouched). *A*, Lip of myocardium below base of cusp, *B*, cusp (supported by black paper), *C*, pulmonary arterial wall.

When aortic cusp homografts (Fig. 9) were used to replace the resected pulmonary cusp, a method was adopted which involved the least risk of damage to the base of the cusp since it lies in close proximity to the rim of annulus where the suturing must be done. Fig. 10 illustrates the trimmed graft (cusp side up) pinned to a piece of cork which is mounted on a fan-shaped metal suture plate. Individual sutures of 00000 arterial silk were taken in the annulus and secured to the suture plate with pinch clips. The graft was then sutured in place with the interrupted technique being used where there was danger of damaging the cusp. A running everting mattress suture of arterial silk completed the suture line (Fig. 8). The clamp was then removed and the ventricular incision closed with several interrupted silk sutures.

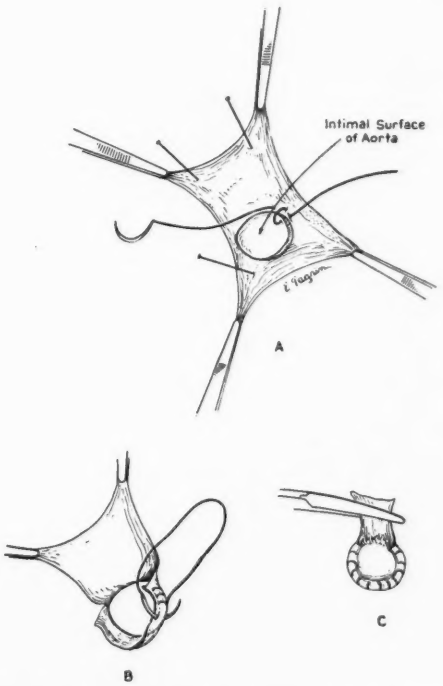


Fig. 12.—Method of prepara ion of the organic cusp prostheses. *A*, Aortic ellipse lying on pericardium, *B*, pericardium sutured to intimal margin of aortic graft, *C*, completed prosthesis.

A simpler technique was possible with the use of pulmonary valvular homografts. The donor cusp was prepared so that a lip of myocardium was left below the base of the cusp (Fig. 11). Therefore, it was possible to rapidly suture the graft in with a continuous type of suture even in those areas close to the cusp.

The second method of pulmonary valvular restoration is the creation of an organic cusp prosthesis fashioned from autograft pericardium and a homograft segment of aortic wall. Fig. 12 illustrates the basic steps in the preparation of the prosthesis. The aorta was trimmed to form an ellipse having slightly more length than one-half of the external diameter of the base of the pulmonary artery and slightly more width than a single sinus of Valsalva. Utilizing these two measurements, both of which were readily obtained, made the aortic ellipse slightly oversized in both length and width in respect to any single cusp of the pul-

monary valve. The adventitia of the aorta was now stripped away. A portion of pericardium, free from fat, was then resected and pinned to a board with the serous side down. The aortic ellipse was placed on the pericardium with the intimal surface of the aorta exposed. A running suture of 00000 arterial silk was employed to suture the pericardium to the margins of the intimal surface of the aortic graft and the knot buried between pericardium and aorta. The excess pericardium was trimmed as necessary. The completed organic cusp prosthesis posessed a serous pericardial surface (autograft) and an intimal (homograft) surface.

Fig. 13 illustrates the various steps in excision of the anterior pulmonary cusp and replacement by the organic cusp prosthesis. A transverse incision was made approximately 3 mm. distal to the annulus. This placed the incision slightly distal to the lunular edge of the

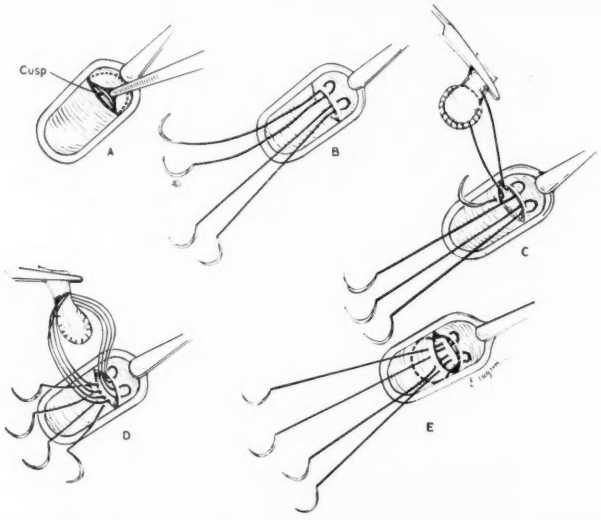


Fig. 13.—Excision of anterior pulmonary cusp and insertion of organic cusp prosthesis (viewed from pulmonary arterial aspect).

A, Transverse incision distal to annulus revealing underlying baffle and anterior pulmonary cusp.

B, Cusp excised and proximal half of horizontal mattress sutures in place.

C and *D*, Sutures fed through pericardium and distal lip of incision.

E, Organic prosthesis interposed between pulmonary arterial wall and baffle.

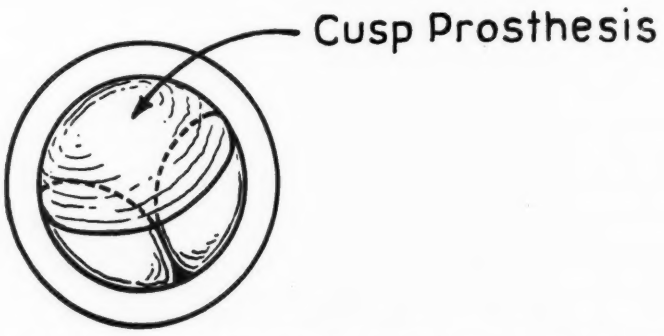


Fig. 14.—Cusp prosthesis, drawn from pulmonary arterial aspect, illustrating method of insuring competency by bolstering effect of unresected cusps.

cusp which was then readily visualized and excised. Several horizontal mattress sutures of arterial silk with atraumatic needles swaged on both ends were begun on the proximal lip of the incision (Fig. 13*B*). These were then fed through the pericardium of the graft approximately 4 mm. from the edge of the aortic ellipse and then through the distal lip of the incision. By grasping the distal ends of the sutures, the prosthesis was easily pulled into place and slipped between the pulmonary arterial wall and the convex baffle. (Fig. 13*E*). The mattress sutures were then tied. Additional interrupted sutures were placed as required and the clamp removed.

Several points bear stressing. The transverse incision must be made slightly distal to the lunular edge of the cusp. This insures free motion of the prosthesis during ventricular systole and competency during diastole, since the oversized prosthesis is supported immediately from behind by the lunular edges of the two remaining cusps (Fig. 14).

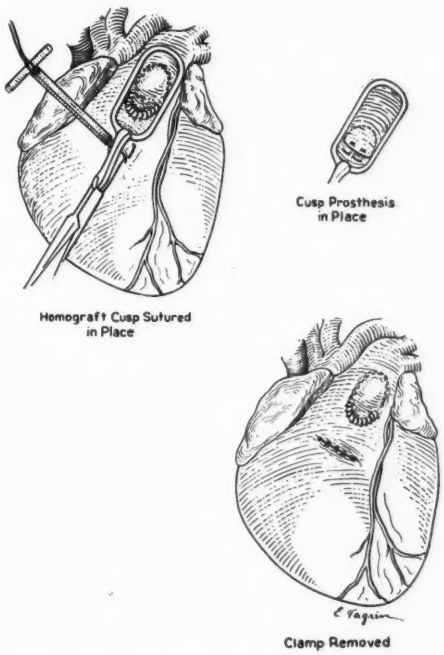


Fig. 15.—Illustration showing homograft cusp and cusp prosthesis at completion of operation.

A second point of importance is the necessity of leaving a margin of approximately 4 mm. between the edge of the aortic ellipse and the point of entrance of the sutures into the pericardium. An inadequate hinging motion of the prosthesis will occur if the sutures are passed too close to the ellipse. Thus, there will be some obstruction to systolic ejection. On the other hand, too great a distance will permit twisting of the prosthesis on the pericardial pedicle with resultant regurgitation.

Fig. 15 illustrates the homograft cusp and cusp prosthesis at the completion of the operation.

AORTIC STENOSIS

The first attempt to correct aortic stenosis surgically was made in 1912 by Tuffier.[10] It was his desire to divide the aortic valve with a knife by entering

the aorta just above the valve ring, but he thought that sufficient experimental data to warrant clinical application were lacking. Therefore an attempt to dilate the stenosed valve was made by invagination of the aortic wall into the ring of the aortic valve. The patient survived and was reported to be still living in 1920.

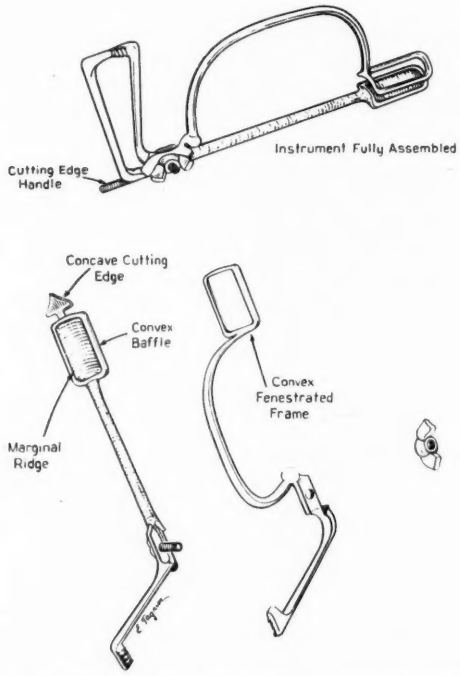


Fig. 16.—Instrument used in aortic valve resection and replacement.

The late Dr. Horace G. Smithy carried out extensive experimentation with transaortic and transventricular aortic valvulotomy.[11, 12]

Recently, Bailey and associates[13] have described both a transaortic and transventricular method of valvular dilatation and transventricular vulvulotomy.

We have attacked the aortic valve utilizing the same approach of cusp excision and replacement as was carried out on the pulmonary valve.

Fig. 16 illustrates the various components of the instrument utilized in aortic cusp resections. The basic principle is unchanged from that seen previously in the pulmonary instrument. As before, there are three basic elements. The first is a convex solid baffle which is rimmed with an elevated marginal ridge. The importance of this ridge will be brought out later. Directly underlying the baffle is a concave cutting edge which is tunneled through the arm proximal to the baffle. Extension of the cutting edge is limited to one-half inch and it is

retained under the baffle by a simple spring mechanism when not in use. The third part of the clamp is a convex fenestrated frame which firmly approximates the marginal ridge of the baffle when the clamp is locked. Its proximal connecting arm is dome shaped. The baffle and fenestrated frame can readily be assembled by the use of a wing nut and bolt, as illustrated.

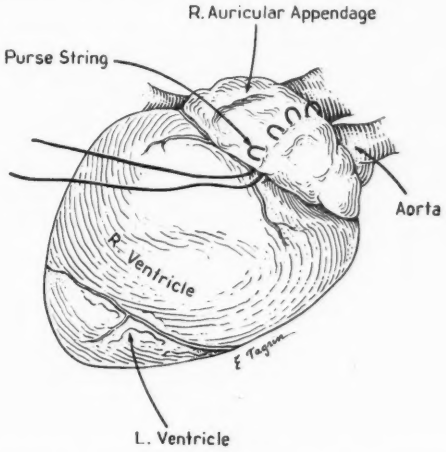


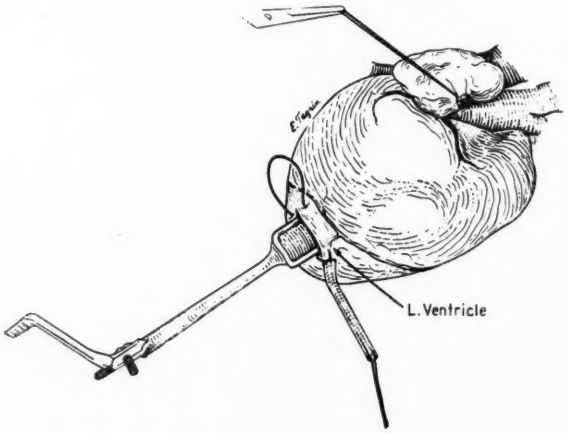
Fig. 17.—Purse-string suture applied at base of right auricular appendage.

METHOD

The chest was entered through the right fifth intercostal space. The sixth rib was divided anteriorly at its costochondral articulation. The pericardium was then opened widely, revealing the apex of the left ventricle, the lateral aspect of the right ventricle and the ascending aorta, a large part of which is hidden behind the right auricular appendage. The free edges of the pericardium are marsupialized to improve exposure. A purse-string suture of 00 braided silk was placed at the base of the right auricular appendage. (Fig. 17). Because of the proximity of the sinoatrial node to the purse-string suture, transient arrhythmias were often noted at this point but these were inconsequential. The appendage was then amputated, immediately bringing into view practically the entire ascending aorta. A purse-string suture of 0 braided silk was then placed in the apex of the left ventricle and the ends passed through a glass tube, as described previously. An incision, approximately 1.5 cm. long, was then made by sharp-pointed iris scissors between the sutures. The convex baffle, the first half of the aortic clamp (with its attached semilunar cutting edge) was rapidly inserted into the left ventricle (Fig. 18). The purse-string suture was then tightened and secured in the same manner as was done with the insertion of the pulmonary instrument. The second part of the clamp (the fenestrated frame) was then placed over the area of the posterior (non-coronary) cusp of the aortic valve which directly underlies the posterior sinus of Valsalva. The clamp was maintained in this position by an assistant. The convex baffle and cutting edge were then carefully guided along the interventricular septum toward the posterior cusp as outlined by the fenestrated frame. As the level of the posterior cusp was approached, the semilunar cutting edge was advanced until the baffle had passed through the valve ring. The cutting edge was then permitted to retract under the baffle. The two parts of the clamp were then slipped together and the wing nut applied. The clamp was then locked, impinging the posterior aortic cusp and its overlying wall between the baffle and the fenestrated frame (Fig. 19). The cusp may now be excised under direct vision.

Both aortic cusp homografts and organic cusp prostheses have been utilized in reconstitution of the aortic valve. During early pilot experiments in which cusp prostheses were inserted into the aortic valve, it was found that the aorta was held so tightly between the baffle and fenestrated frame that attempts at slipping the prosthesis between the aorta and the baffle always resulted in the aorta being torn. Therefore, the marginal ridge was added to the instrument. This had the effect of depressing the central portion of the baffle and thus provided a slot into which the prosthesis could readily be inserted. The details of each technique are precisely the same as those described previously in pulmonary cusp replacement.

In insertion of the aortic cusp homografts, it was not possible to align the lunular edges of the cusps. This was due to the fact that correct insertion of a homograft cusp requires not only removal of the cusp itself but excision of several millimeters of tissue proximal to the base of the cusp to offset the marginal bit of tissue which must be left for suturing purposes below the base of the cusp to be grafted. Therefore, it was necessary for the instrument to provide visualization of as much as one-half centimeter below the base of the cusp. This provided no problem in insertion of homograft cusps into the pulmonary valve since no vital structures lie proximal to the anterior pulmonary cusp. However, attempts to visualize the area below the base of the posterior aortic cusp resulted in impingement of



INSERTION OF 1ST HALF OF CLAMP
WITH CUTTING EDGE

Fig. 18.—For description, see text.

the interventricular septum by the instrument at a point almost directly overlying the atrioventricular bundle. Secondly, severe deformity of the right atrium occurred with this maneuver and right ventricular filling was impaired. Almost immediately, a severe bradycardia or bizarre arrhythmia occurred and this was followed by ventricular fibrillation or cardiac arrest.

No such problem was encountered in insertion of organic cusp prostheses into the aortic valve since visualization of the cusp alone is required. Using this technique, no suturing was required at the base of the resected cusp, all work being done at the site of the leading (lunular) edge which could be readily visualized and isolated. The completed procedures are illustrated in Fig. 19.

RESULTS OF PULMONARY CUSP REPLACEMENT

Thirty-one animals were subjected to pulmonary cusp replacement. The results of these operations are shown in Tables I and II. Twenty-two homo-

graft cusps and 9 organic cusp prostheses have been inserted. There were four operative deaths. Three of these were from hemorrhage and one from ventricular fibrillation. There were an additional three deaths due to atelectasis, two from distemper and one from cerebral anoxia due to mechanical failure of the endotracheal cuff.

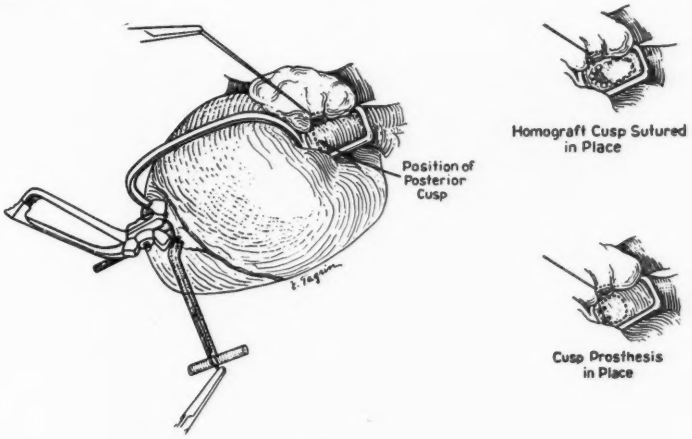


Fig. 19.—Clamp in position. Note approximate position of posterior cusp. Also shown are the two methods of cusp replacement at operative completion.

Fig. 20.—Specimen one and one-half months after grafting (Dog 6). There is thickening and fixation of cusp. Positioning of cusp is poor.

The remaining twenty-one animals were sacrificed at intervals varying from five days to ten months postoperatively. In all cases, retrograde perfusion of saline under pressure was used to determine valvular competency. At sacrifice, electrocardiograms and phonocardiograms were taken.

All homograft cusps of animals who died immediately postoperatively and of Dog 3 (sacrificed at five days) appeared delicate and pliable. Valvular competency was observed in each of these animals except Dog 2. In this case, the valve had been placed too low. The homograft cusps which were in place for longer periods of time were totally incapable of functioning as competent cusps, with three exceptions.

Fig. 21*A*.—Specimen four months after grafting (Dog 31). Note shrinkage and retraction of cusp.

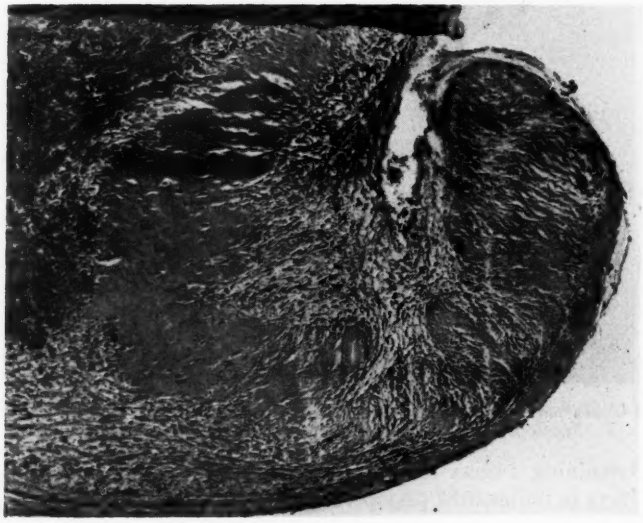


Fig. 21*B*.—Photomicrograph of cusp embedded within connective tissue and undergoing organization (×90).

The degenerative process appeared to be one of initial thickening and fixation of the cusp due to fibroblastic proliferation (Fig. 20). Later, there was marked shrinkage and retraction (Fig. 21). The final stage was one in which only the slightest vestige of the cusp remained (Fig. 22). The microscopic features of this process are shown in Fig. 21*B*. The cusp was com-

Fig. 22.

Fig. 23*A*.

Fig. 22.—Specimen ten months after grafting. Only the slightest vestige of a cusp is evident.

Fig. 23*A*.—Specimen seven months after grafting. The cusp is thin and delicate. Directly beneath the graft is an organizing thrombus situated at the sight of the ventricular incision.

pletely embedded within loose connective tissue and organizing blood clot. The leaflet persisted as a necrotic, shadowy outline undergoing organization. There was a marked inflammatory reaction throughout the graft.

In contrast to these failures was the one apparently successful graft of Dog 12 (seven months, Fig. 23). The grafted cusp appeared thin and delicate and did not seem to have undergone any gross change. Retrograde perfusion of saline demonstrated competency of the valve. Fig. 23, *B* and *C* shows the microscopic appearance of the grafted cusp of Dog 12. The lines of apposition showed minimal chronic reaction. The cusp was delicate, well preserved, and without inflammatory reaction or scarring. Special stains showed some slight loss of elastic tissue but the persistence of a fine network of elastic fibrils within the valve leaflet.

Fig. 23*B*.

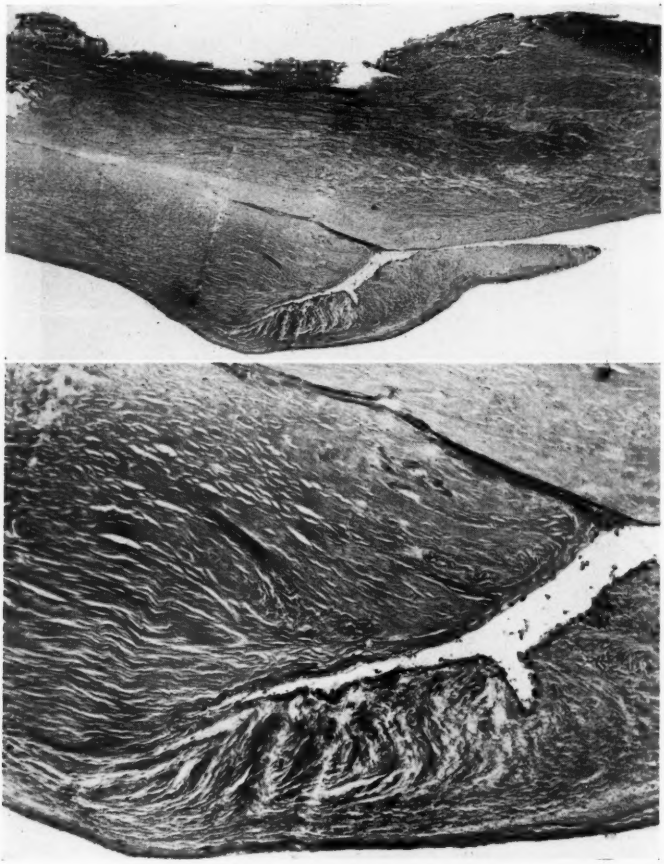


Fig. 23*C*.

Fig. 23*B*.—Photomicrograph (×40). The cusp is delicate and well preserved.
Fig. 23*C*.—Higher power Photomicrograph (×90). The cusp is without inflammatory reaction or scarring.

Animals having pulmonary cusp replacement with organic cusp prostheses were autopsied from three weeks to seven months postoperatively (Table II). All prostheses were well placed and preserved. Only one valve was incompetent. In this animal (Dog 29), the cusp had been made too small and swung freely on its pericardial hinge.

Fig. 24*A*.

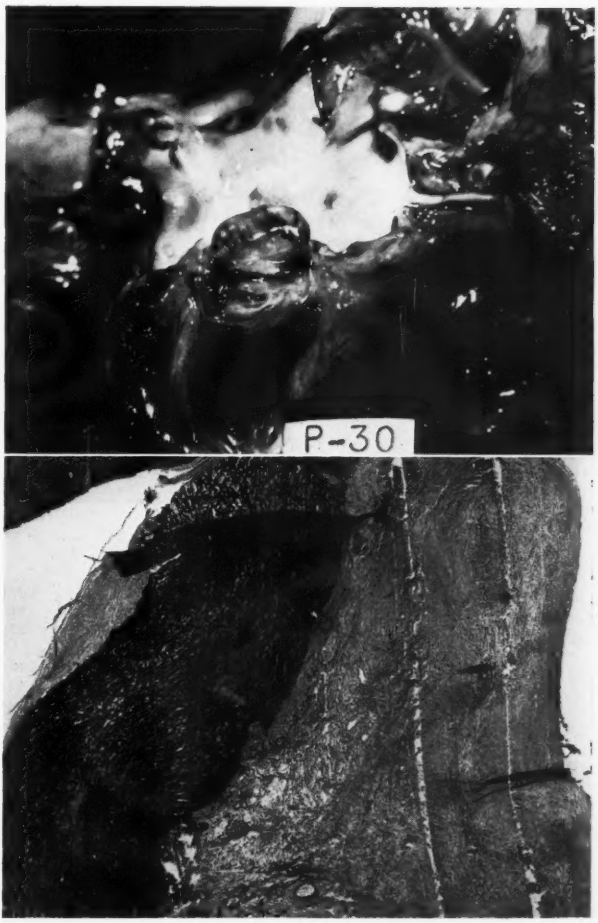


Fig. 24*B*.

Fig. 24*A*.—Organic cusp prosthesis of animal sacrificed at four and one-half months. Note excised cusp.

Fig. 24*B*.—Photomicrograph of prosthesis. Inflammatory connective tissue is present between the aortic graft and pericardium. The aorta is well preserved (elastic tissue stain ×80).

Fig. 24 shows a prosthesis four and one-half months after insertion (Dog 30). All the prostheses appeared slightly thicker than they were at the time of surgery. Microscopically, this thickening appeared to be due to the accumulation of inflammatory connective tissue between the pericardium and the aortic graft (Fig. 24*B*). The aortic grafts themselves showed good preservation of structure.

Fig. 25*A*.

Fig. 25*B*.

Fig. 25*A*.—Homograft cusp in aortic valve one month after surgery (cusp supported by cardboard for photographic purposes). Note poor positioning of cusp.

Fig. 25*B*.—High-power photomicrograph. Active connective tissue surrounds and is invading the leaflet.

RESULTS OF AORTIC CUSP REPLACEMENT

Twenty-one animals were subjected to aortic cusp replacement (Tables III and IV). Nine homograft cusps and twelve organic prostheses were inserted.

There were two operative deaths, one from cardiac arrest and one from hemorrhage. An additional two deaths occurred on the first postoperative day due to atelectasis.

The remaining seventeen dogs were sacrificed at intervals varying from one week to four and one-half months. Prior to sacrifice, arterial pressure tracings were obtained using a Sanborn electromanometer as well as electrocardiograms and phonocardiograms. After sacrifice, competency was tested by retrograde saline perfusion under pressure. The autopsy studies corroborated the findings seen in the pulmonary group.

TABLE I. RESULTS OF PULMONARY CUSP REPLACEMENT WITH HOMOGRAFT CUSPS

DOG	CUSP INSERTED	SURVIVAL TIME	PHONOCARDIOGRAM	CONDITION OF CUSP	COMPETENCY AT SACRIFICE
1	Aortic	8.5 mo.	Systolic	Shrunken and fibrotic	No
2	Aortic	1 day, atelectasis		Thin and delicate	No
3	Aortic	5 days	No murmur	Thin and delicate	Yes
4	Aortic	10 mo.	Systolic, diastolic (?)	Thickened vestige	No
5	Aortic	Operative death, hemorrhage			
6	Aortic	1.5 mo.	Systolic and diastolic	Thickened, fixed	No
7	Aortic	1 mo.	Systolic	Thickened, shrunken	No
8	Aortic	4 mo., death from distemper	No examination		
9	Aortic	8 mo.	Systolic and diastolic	Thickened vestige	No
10	Pulmonary	4.5 mo.	Early systolic	Thin and delicate	Yes
11	Pulmonary	Operative death, hemorrhage			
12	Pulmonary	7 mo.	Systolic	Thin and delicate	Yes
15	Pulmonary	1 day, atelectasis		Thin and delicate	Yes
16	Pulmonary	6 mo.	Systolic	Thickened vestige	No
17	Pulmonary	Operative death, hemorrhage			
18	Pulmonary	4 mo.	Systolic and diastolic	Shrunken, retracted	No
20	Pulmonary	3 weeks	Systolic	Thickened, fixed	No
22	Pulmonary	1 day, cerebral anoxia		Thin and delicate	Yes
25	Pulmonary	3 mo.	Systolic	Vestige	No
27	Pulmonary	3 weeks	No murmur	Thin and delicate	Yes
28	Pulmonary	1 day, atelectasis		Thin and delicate	Yes
31	Pulmonary	4 mo.	Systolic	Thin, shrunken	?

TABLE II. RESULTS OF PULMONARY CUSP REPLACEMENT WITH CUSP PROSTHESES

DOG	SURVIVAL TIME	PHONOCARDIOGRAM	CONDITION OF CUSP	COMPETENCY AT SACRIFICE
13	7 mo.	Systolic	Good	Yes
14	19 days, death from distemper		Good	Yes
19	1 mo.	Systolic	Good	Yes
21	3 weeks	Systolic	Good	Yes
23	2.5 mo.	Systolic	Good	Yes
24	6 mo.	No murmur	Good	Yes
26	0, ventricular fibrillation as chest closed		Good	Yes
29	2 mo.	Systolic and diastolic	Cusp too small	No
30	4.5 mo.	Systolic	Good	Yes

All homograft cusps of the dogs who either died immediately postoperatively or were sacrificed within a short time appeared thin and delicate. Cusps in place for longer periods of time appeared shrunken. All the grafted cusps had been positioned distal to the lunular edges of the recipients' own cusps. Therefore, incompetency resulted from faulty positioning as well as shrinkage of the cusps in the older animals.

Fig. 25 illustrates the typical finding of a poorly positioned posterior cusp in an animal sacrificed one month after operation. Despite the fact that the cusp appeared thin and delicate, the photomicrograph reveals that the cusp is somewhat degenerated with a thin covering of active connective tissue which is invading the leaflet. There is evidence of persistence of necrotic tissue.

Animals having aortic cusp replacement with organic cusp prostheses were sacrificed at intervals between one week and four and one-half months (Table IV). All prostheses were well positioned. Competency was observed in all animals except Dog 4. Clinically, the animal appeared listless almost immediately after operation and was sacrificed twenty-one days later. Examination revealed that the aortic wall was fragmented directly overlying the prosthesis and that a perforation had occurred into the right atrium with the creation of an aortoatrial fistula. The cusp was overlying the fistula and was covered with a thrombus.

TABLE III. RESULTS OF AORTIC CUSP REPLACEMENT WITH HOMOGRAFT AORTIC CUSPS

DOG	SURVIVAL TIME	PHONOCARDIOGRAM	POSITION	CONDITION OF CUSP	COMPETENCY AT SACRIFICE
1	1 mo.	Diastolic	Poor	Shrunken	No
2	1 day, atelectasis		Poor	Thin and delicate	No
3	3 mo.	Systolic	Poor	Shrunken	No
5	1 day, atelectasis		Poor	Thin and delicate	No
6	1 week	Systolic	Poor	Thin and delicate	No
7	1 mo.	Systolic and diastolic	Poor	Shrunken	No
9	2 mo.	Systolic and diastolic	Poor	Shrunken	No
18	1 mo.	Systolic	Poor	Thin and delicate	No
19	1 mo.	Diastolic	Poor	Thin and delicate	No

TABLE IV. RESULTS OF AORTIC CUSP REPLACEMENT WITH CUSP PROSTHESES

DOG	SURVIVAL TIME	PHONOCARDIOGRAM	CONDITION OF CUSP	FUNCTION
4	3 weeks	Systolic and diastolic	Poor	No
8	4.5 mo.	Early systolic	Good	Yes
10	Operative death, cardiac arrest			
11	Operative death, hemorrhage			
12	3 mo.	Systolic	Good	Yes
13	1.5 mo.	No murmur	Good	Yes
14	1 week	Systolic	Good	Yes
15	1 mo.	No murmur	Good	Yes
16	3 weeks	Systolic	Slight ballooning	Yes
17	1 mo.	Systolic	Good	Yes
20	1 mo.	Systolic	Good	Yes
21	4.5 mo.	Systolic	Good	Yes

Fig. 26*A*.

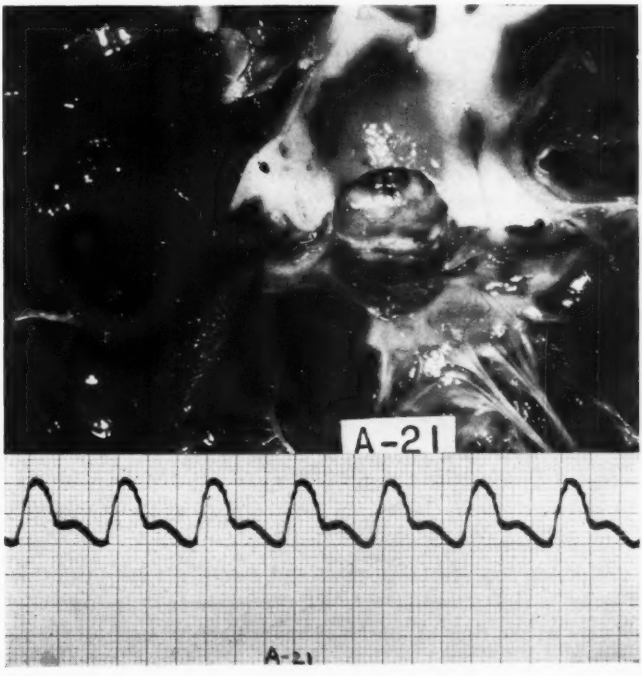


Fig. 26*B*.

Fig. 26*A*.—Cusp prosthesis in aortic valve in animal sacrificed four and one-half months after surgery.

Fig. 26*B*.—Aortic pressure tracing done prior to sacrifice. There is no evidence of insufficiency or systolic obstruction.

In all other animals the prostheses appeared satisfactory in all respects. They all appeared slightly thicker than at the time of insertion and, microscopically, this again was demonstrated to be a result of the presence of inflammatory connective tissue between the aorta and the pericardium.

Fig. 26*A* is a photograph of an organic cusp prosthesis inserted four and one-half months prior to sacrifice. The cusp is slightly thicker than at the time of surgery. The arterial tracing (done at the time of sacrifice) is seen in Fig. 26*B*.

DISCUSSION

To date, intracardiac surgery of pulmonary and aortic valvular stenosis has been confined to blind incision and dilatation of the valve. Functional restoration, therefore, is dependent upon residual flexibility of the valve. If the pathologic process has rendered the valve rigid and calcific, these procedures may produce only limited improvement. Thus, the limiting factor is the state of the valve itself.

Resection of a portion of the valve would permit permanent maintenance of an adequate outflow tract regardless of the condition of the valve. It is axiomatic, however, that any partial valvular resection cannot be carried out at the expense of creation of a regurgitant lesion. Experimental[1] and clinical[13] data have shown that the effect of a suddenly imposed aortic regurgitant lesion is highly detrimental and is disastrous in the diseased human heart. It is probable that a moderate amount of surgically imposed pulmonary regurgitation may be tolerated. That this may not always be the case is illustrated by the report of Glover and associates.[14]

It would seem, therefore, that surgical excision of a portion of the valve combined with adequate means of control of regurgitation is a logical approach to the problem of stenotic lesions of the semilunar valves. The advantages of doing the surgery under direct vision with uninterrupted blood flow are apparent.

The results with the use of homograft pulmonary and aortic cusps have been disappointing and are in agreement with the reports of Bill and associates,[15] Hufnagel,[16] and Lam and associates.[17] While the degenerative process may vary in terms of time, the end result is fibrosis and shrinkage of the cusp. It is difficult to speculate upon the reason for the apparently successful grafting of Dog 12 (Fig. 23*A*).

The use of the combined autograft and homograft cusp prostheses has been more successful in the time observed. All the specimens appeared slightly thicker than they were at the time of insertion but seemed to meet all the requirements for functional cusps. Retrograde perfusion studies and arterial tracings demonstrated that they could adequately prevent regurgitation. Since it is possible to create any desired size of prosthesis, one might speculatively suggest the application of this method for the control of associated regurgitant lesions, especially of the aortic valve, since incompetency so frequently augments the problem of the valvular stenosis.

Many questions remain to be answered. The effectiveness of the operation on the diseased human heart remains to be determined. Moreover, the long term efficiency of the autograft-homograft prostheses is still unknown.

SUMMARY

1. An approach for the surgical relief of stenotic lesions of the semilunar valves is presented.

2. Instruments are described which permit excision of one-third of either the aortic or the pulmonary valve (one cusp) and adjacent vascular wall. This may be done under direct vision without interruption of the circulation.

3. Valvular reconstitution has been carried out with homograft aortic and pulmonary cusps and also organic cusp prostheses.

4. The use of homografted cusps is entirely unsatisfactory.

5. The organic cusp prostheses functionally act as competent flap valves.

The authors would like to express their appreciation for the guidance of Dr. George L. Maison, Dr. Robert O. Bauer and Dr. Jacob W. Stutzman. We are greatly indebted to Mrs. Edith Tagrin for the numerous illustrations. We are grateful to Dr. Stanley L. Robbins for reviewing the histologic sections. Dr. N. Robert Frank, Mr. Edward Swiss, Mr. Abraham Kaplan and Miss Lois Mosey carried out the physiological studies. We should also like to thank Mr. Duncan Campbell for aid in operating on the dogs. Appreciation is also expressed to Dr. James L. Harrison for his valuable suggestions and criticisms.

The instruments were made by Mr. Everett Kellogg, the Universal Tool and Die Co., Somerville, Mass., and the Globe Tool and Gage Works, Boston, Mass.

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EXPERIMENTAL PULMONARY VENOUS OCCLUSION

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THIS report presents a study of the survival or death of dogs subjected to division of the pulmonary veins from one lung. It has been thought that a fatal result uniformly follows such complete unilateral division of the pulmonary veins. However, in 1940, Hyndman and associates,[1] studying the effect of pulmonary congestion on tuberculosis in the dog, remarked that ligature of all the veins on the left at one operation was "not in the least incompatible with life." In 1948, Swan and Mulligan[2] reported the effects of division of pulmonary veins in dogs. These investigators observed that healthy dogs survive indefinitely following division of the pulmonary veins from one lobe. However, complete ligation of the pulmonary veins from one lung was fatal in two dogs which they reported. One of these animals died twenty-four hours after division of the left pulmonary veins, the other died three days after division of the right pulmonary veins. These latter authors reasoned that dogs with lobar ligations survived whereas those with total unilateral ligations died because of a quantitative difference between the two procedures related to the volume of blood loss as pulmonary hemorrhage.

Our own unreported experience with lobar vein ligations corroborated the excellent studies of Swan and Mulligan. However, it was noted in other similar experiments that certain dogs survived even when the venous return from an entire lung was divided. Being unaware at that time of the work of Hyndman and associates,[1] it was presumed that penicillin might have exerted a favorable effect on the course of these animals. The present study was performed to provide a quantitative assessment of the hypothesis that penicillin exerted a mitigating effect on the mortality rate in pulmonary venous occlusion.

METHODS

Healthy, adult mongrel dogs were used, varying in weight from 6 to 14 kilograms. They were fed on stock diet of dry dog biscuit and water and kept in individual cages throughout the experiment. Anesthesia was induced with intravenous sodium pentobarbital after preliminary medication with morphine and atropine. The total dosage of sodium pentobarbital did not exceed 30 mg./kg. of body weight; most of this was given intravenously until the dog became unconscious, after which the animal was usually given a small additional intramuscular dose. Pulmonary ventilation was maintained by intermittent insufflation of oxygen through a sterilized endotracheal tube with inflated

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cuff. In a few of the earlier animals in the series, small amounts of ether vapor were employed for maintenance. All of the animals awoke promptly at the conclusion of the operative procedure and were allowed diet and water as desired. The rapidity with which normal eating habits were resumed was of some prognostic significance; a dog which was eating normally within one or two days usually recovered.

Aseptic, "silk" technique was employed throughout. The chest was entered by an intercostal incision on either side, usually through the fifth intercostal space. The pulmonary veins were isolated extrapericardially at the hilum of the lung and were divided between transfixion ligatures. Closure of the chest was performed in layers without drainage. At the conclusion of the procedure a single hypodermoclysis of normal saline solution was given in the amount of 30 c.c./kg. of body weight. No further supportive therapy was employed except in the animals of the penicillin-treated group. The agent used was crystalline penicillin "G" in a dosage of 20,000 units/kg. of body weight. It was given intramuscularly at the conclusion of operation and at daily intervals thereafter until the animals resumed their diet and were clearly on the way to recovery. Administration of penicillin was continued for a period of two to five days with an average of three days.

In ten animals blood cultures were taken and maintained under both aerobic and anaerobic conditions. Autopsies were performed on all animals promptly after death. Confirmation of the completeness of pulmonary venous interruption was secured in all instances. Photographs of the gross specimens were made and sections were taken from representative areas of the lung for histologic study.

RESULTS

Twenty-five dogs were subjected to complete division of the pulmonary veins from one lung. This procedure was performed on the left side in eight animals and on the right side in seventeen. The animals were divided into four groups, the variables being the side of operation and the employment of penicillin therapy after operation.

Group I., Complete Division of the Left Pulmonary Veins With Postoperative Penicillin.—There were four dogs in this initial group. Soon after division of the veins, the lung became dark red and congested but the animal showed no untoward general signs and the immediate postoperative condition was similar to that following simple thoracotomy. The early postoperative days were marked by less than usual spontaneous activity, by a mild cough, and production of small amounts of bloody sputum. Within five days, however, all animals appeared well and penicillin had been discontinued; one dog received the antibiotic for only one day after operation. The dogs were sacrificed at varying periods up to thirteen months after operation.

Comment: The benign clinical course of these animals was at least partially attributed to penicillin. To evaluate this factor, a second group of animals was studied.

Group II., Complete Division of the Left Pulmonary Veins Without Penicillin.—Four dogs made up this group, similar in all respects to the preceding except that penicillin was omitted. All of these animals survived the division of all pulmonary veins on the left side with essentially the same clinical picture presented by those in the penicillin-treated group. At the time of sacrifice, from 5 days to 6 months after operation, the dogs appeared quite well.

Comment: It was obvious that the beneficial effect of penicillin could not be assessed in animals with ligation of the left pulmonary veins, since this procedure was unassociated with any mortality under the conditions of our experiments. In an attempt to impose a more severe strain on the experimental animal, a third group of dogs was studied.

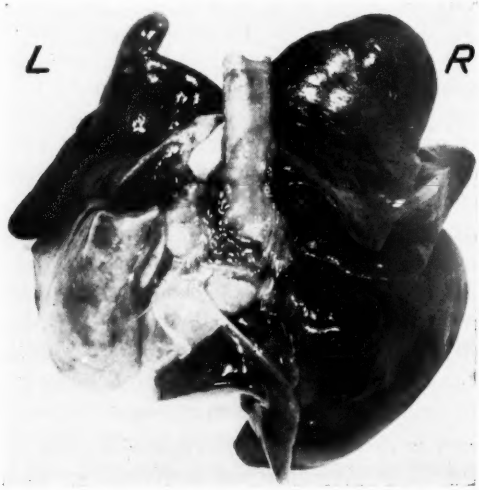

Fig. 1.—Photograph of dog's lung 20 hours after division of right pulmonary veins. Death occurred despite penicillin therapy. Note severe congestion in left upper lobe as well as in entire right lung.

Group III., Complete Division of the Right Pulmonary Veins Without Penicillin.—This group comprised nine dogs, six of which died in from one to ten days, with an average postoperative life of three and a half days. These animals showed a clinical picture of sluggishness, anorexia, and a persistent cough productive of large amounts of bloody, mucoid sputum. In some animals there was extreme orthopnea in the terminal state. In others, increasing torpor was the most prominent feature. One animal appeared on the way to recovery after a week, but developed signs of severe infection and died after ten days with widespread bronchopneumonia in the lung on the operated side. Multiple small abscesses were present in the periphery of this lung. Three of these animals had bacteriologic studies of the blood; all cultures were positive.

Three dogs with all of the right pulmonary veins divided did not die although their postoperative course was quite stormy. In two of these animals

blood cultures were taken; one had a single positive culture on the day after operation and the other had bacteriologic proof of septicemia on five occasions during the first two weeks following surgery. Both are alive several months after ligation.

Comment: This group of animals demonstrates that under the stated conditions there is a high but not invariable mortality associated with total interruption of the right pulmonary veins. It appears likely that infection may play a part in the unfavorable course of these untreated animals. The positive blood cultures also suggest a logical reason for the use of antibiotic therapy.

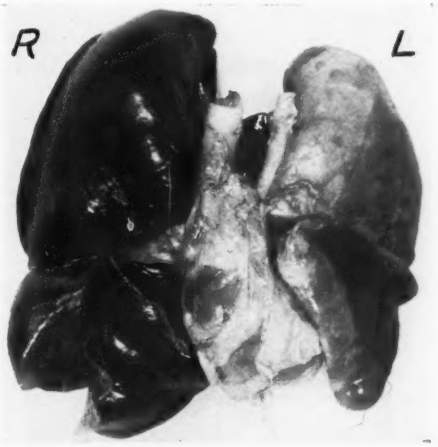

Fig. 2.—Thoracic viscera of dog sacrificed 24 hours after division of right pulmonary veins. Intense congestion of right lung is present.

Group IV., Complete Division of the Right Pulmonary Veins With Postoperative Penicillin.—There were eight animals in this group of which seven survived. In the one dog which died after 20 hours, the entire right lung was congested as would be expected, but there was in addition a similar involvement of the left upper lobe (Fig. 1). It is possible that this additional involvement, presumably due to atelectasis from inhaled secretions of the contralateral lung, led to quantitative insufficiency of ventilated alveoli. A single blood culture in this animal was negative. The picture in this animal may be compared with that seen in an animal sacrificed for pathologic study 24 hours after division of the pulmonary veins from the right lung (Fig. 2). In this latter animal, which was progressing satisfactorily, the entire right lung was solidified but there was no comparable change on the left. A portion of the left lower lobe was slightly congested but still air-containing. At 10 days after operation there is no sign of gross alteration in the opposite lung, as seen in Fig. 3. The right lung is beginning to clear in its lower portion.

This process of clearing goes on steadily, as seen in the lungs of a dog sacrificed one month after interruption of the right pulmonary veins (Fig. 4). The affected lung is now more than half expanded, with intervening areas of atelectasis and incomplete resolution of hemorrhagic congestion. The process in the entire lung varies but little from that which has been known to occur during resolution of congestion in single lobes. Details of the mechanism of clearing will be reported elsewhere.[3]

By 10 weeks after ligation of the right pulmonary veins in penicillin-treated animals, there is fairly good pulmonary expansion (Fig. 5). This is complete in the lower portion of the lung but cannot be demonstrated in the upper portion because of tears in the pulmonary parenchyma associated with division of adhesions over the right upper lobe. After 6 months the lung is fully air-containing but somewhat contracted with a moderate degree of diffuse interstitial fibrosis (Fig. 9).

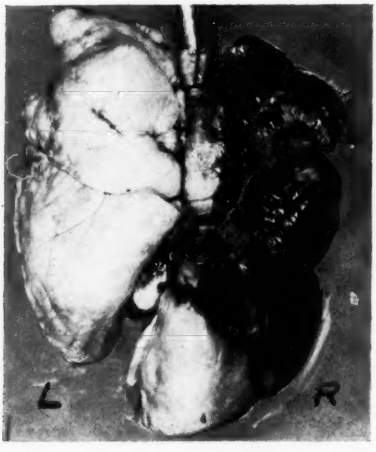

Fig. 3.—Lungs of dog 10 days after division of right pulmonary veins. Congestion of right lung beginning to clear at lower portion.

The histologic changes at various periods after ligation are correlated with the gross appearance of the lung. After 24 hours (Fig. 6) the pulmonary parenchyma is stuffed with red cells and leukocytes so that the normal architecture of the lung is barely discernible. By 10 days after ligation (Fig. 7) the pleura shows an organizing fibrinous exudate, and macrophages filled with hemosiderin are prominent in the unaerated pulmonary parenchyma.

After 1 month (Fig. 8) the alveolar ventilation is much improved with focal areas of fibrosis distributed widely throughout the parenchyma. After 6 months (Fig. 9) the picture is one of complete aeration but there is diffuse thickening of alveolar septa.

Comment: When penicillin is given after total interruption of the right pulmonary veins the mortality rate (12.5 per cent) is appreciably less than in the untreated group (66.6 per cent). These groups are small, and the mortality figures may be taken as indicative of a trend rather than as an absolute index of antibiotic efficacy in pulmonary venous congestion.

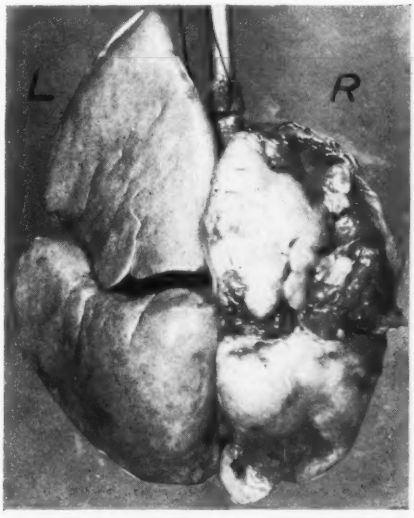

Fig. 4.—Lungs of dog 1 month after division of right pulmonary veins. Pale areas of right lung represent aerated portion with darker intervening areas of atelectasis and congestion.

Fig. 5.—Ten weeks after division of right pulmonary veins there is expansion of lower portion of right lung with collapse of upper portion due to tear of pulmonary parenchyma associated with division of adhesions during removal. Note thickened pleura over interlobar fissure.

DISCUSSION

It is apparent that ligation of all the pulmonary veins from one lung of the dog, while extremely disturbing in many instances and fatal in some, is nonetheless survived by certain animals. All of our animals have survived when this procedure was performed on the left side. When the right pulmonary veins are totally interrupted, however, the mortality rate has been quite high, possibly because the operative insult is inflicted on an appreciably larger volume of pulmonary tissue. It has been known that ligation of the veins from a single pulmonary lobe is tolerated by the dog. We have corroborated the observation

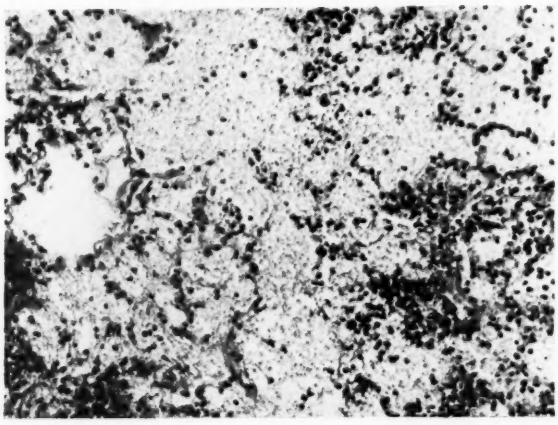

Fig. 6.—Division of right pulmonary veins 24 hours previously. Note intense congestion of pulmonary parenchyma with erythrocytes. Alveolar outlines are indistinct (Hematoxylin and eosin ×210).

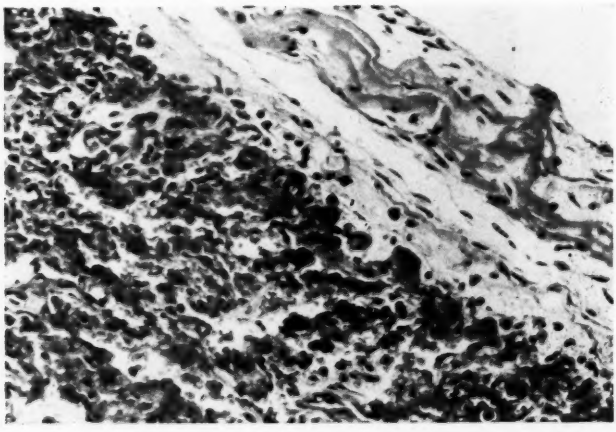

Fig. 7.—Division of right pulmonary veins 10 days previously. Note fibrinous pleural exudate and hemosiderin-filled macrophages in unaerated alveoli (Hematoxylin and eosin ×380).

that the entire left lung may be similarly treated without overtaxing the compensatory mechanisms by which the animal usually adjusts to such venous interruption.

If one administers penicillin postoperatively to those animals whose right pulmonary veins have been interrupted, the survival rate is increased, for reasons which are not immediately obvious. It would appear, however, that

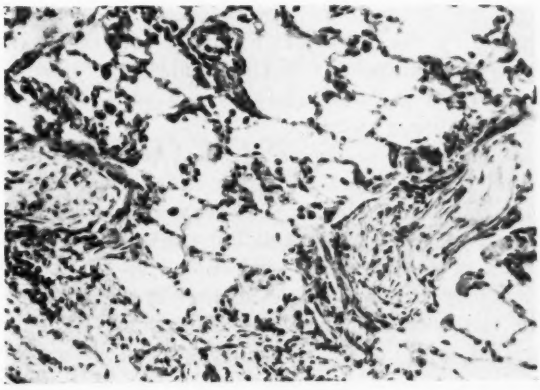

Fig. 8.—Division of right pulmonary veins 1 month previously. Widely distributed areas of focal fibrosis with intervening well-ventilated alveoli.

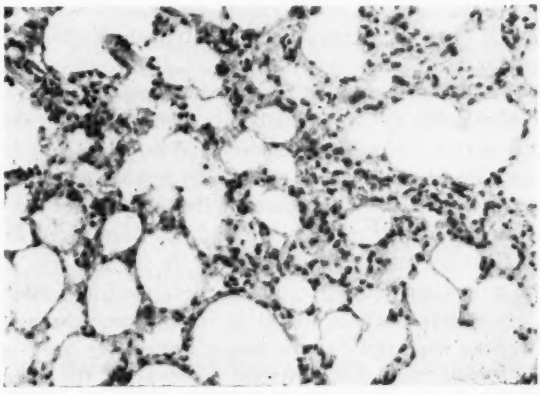

Fig. 9.—Division of right pulmonary veins 6 months previously. Alveoli completely aerated but there is diffuse interstitial fibrosis.

penicillin had altered in some way the usual mechanism resulting in death of these animals.

Three possible explanations of this alteration may be mentioned. First, it is apparent from goss and microscopic examination that a large amount of blood is trapped in the congested lung. Such local fluid loss might well lead to shock, and the increase in weight of the affected lung is consistent with this hy-

pothesis. Although all of our animals received a single hypodermoclysis of normal saline solution after operation, this would not be considered vigorous shock therapy by usual standards. Fluid depletion might well be severe in the ensuing days and critical evaluation of this has not yet been attempted. The moderate depression of the hematocrit in those dogs which survived for a few days does not suggest that acute anemia plays a highly significant role.

A second possible explanation of death in these animals may lie in ventilatory insufficiency. The lung on the side of operation is rendered unfit for respiratory exchange by the blood which fills its parenchyma and overflows into the trachea as bloody sputum. Such sputum may be aspirated into the opposite lung and result in further interference with respiratory exchange until finally the animal dies of anoxia.

Both of these mechanisms—decreased blood volume and respiratory insufficiency—demand critical appraisal, but it is not clear how the beneficial effect of penicillin could be explained if these were the main cause of death in experimental venous occlusion. Penicillin might be expected to have its chief effect on the third possible factor—infection.

That infection plays some role is evidenced by the finding of a positive blood culture in many of the untreated animals and in only one of the treated animals. The origin of these organisms is not clear although there is little doubt that the congested lung provides an excellent medium for their growth. The inhibition of bacterial growth by penicillin might be adduced as the reason for increased survival in treated animals with occlusion of the right pulmonary veins. But if infection is the sole determining factor, it seems strange that it does not exert a similar detrimental effect on the animals with left-sided venous occlusion.

From the data at hand, no positive conclusion may be drawn regarding the precise mechanism of death in our animals. It seems probable that a combination of local fluid loss, ventilatory insufficiency and infection may be responsible.

There are two clinical examples of pulmonary venous interruption to which these studies may be relevant. Ligation of pulmonary veins has been advised in the treatment of pulmonary tuberculosis and has been given limited clinical trial by Edel,[4] Kerschner,[5] and O'Shaughnessy.[6] In the unlikely event that this method of venous congestion should be more widely used, the role of antibiotics in minimizing its untoward effects would be significant. As a more common problem, if the venous drainage from a major pulmonary area is accidentally compromised at surgery, some have advised removal of the affected segment. If the studies reported here may be applied to patients, such advice would seem unduly radical. On the other hand, preliminary physiological studies suggest that a lung which re-expands after such venous congestion is not capable of significant respiratory exchange but is primarily a space-occupying structure. Further study may be expected to clarify the functional status of such a lung.

SUMMARY

Interruption of the entire pulmonary venous return from one lung in dogs is compatible in some instances with prolonged survival. Mortality from such a

procedure is decreased when penicillin is given after operation. The mechanism of this reduction in mortality is discussed. The physiologic implications of the problem are under study.

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DISCUSSION

DR. F. A. HUGHES, Memphis.—We have produced pulmonary venous congestion in the dog experimentally, in relation to pulmonary implantation.

(Slide.) Here is a dog that survived implantation of the left lower lobe. The reason I show this is because this dog has complete occlusion of the veins, pulmonary and all others, and occlusion of the bronchus of the left lower lobe.

(Slide.) The left lower lobe is congested and distended.

(Slide.) Here are the sites of anastomoses of the artery and the vein, and you see the vein is completely occluded; the bronchus was completely occluded also. The artery is not well anastomosed but remains patent. This dog was killed three weeks after operation. The specimens are from the parenchyma of the lobe; this is the normal lobe and this is the lobe subjected to implantation. There is enormous dilatation of the bronchi here.

(Slide.) Here one cannot see the site of anastomosis of an auricle around the vein.

It might be possible for patients to survive easily if a vein were obstructed. I should think that that portion of the lung should preferably be removed. Dr. Hanlon has shown that, in some instances, it would probably be justifiable to give adequate doses of antibiotics.

DR. RALPH D. ALLEY, Albany, N. Y.—Dr. Burke has shown a definite correlation between survival rate and administration of antibiotics. He has not explained the difference in mortality on the two sides, and I would like to suggest that the 100 per cent survival on the left side might be related to the anatomic fact that the venous drainage from the right subcardiac or accessory lobe is usually into the left inferior vein. A ligature about the left inferior vein inadvertently placed distal to the right accessory venous inflow might serve as a venous vent to the nonligated side, and explain the high survival rate on the left side.

The principal reason for my arising, however, is to stress the importance of an hemodynamical variable not mentioned in the control of these experiments. It has been known for many years that the bronchial arterial collateral system of the lungs undergoes great expansion in association with chronic pulmonary disease states. This fact was emphasized by Dr. Emil Holman in the early 1930's and, more recently, Dr. Averill Liebow of New Haven has depicted the changes very strikingly with plastic bronchovascular casts. Very little concerning the bronchial veins has been described beyond the fact that they do exist and drain both into the pulmonary veins and into the azygos system. Recently, in an as yet unpublished work, Dr. Liebow has also shown an expansion of the bronchial venous system accompanying chronic pulmonary disease states. In the light of this knowledge experiments involving the pulmonary circulation are necessarily incompletely controlled unless the bronchial vascular system is taken into account.

For example, although "healthy mongrel dogs" were utilized in these experiments, we do not know their medical background. The usual batch of laboratory animals represents a cross-sectional sampling of the full spectrum of canine socioeconomic groups with, if anything, a more generous proportion of former canine vagrants. The latter, under conditions of privation earlier in their careers, may have had episodes of distemper and pneumonitis which left their mark of an expanded bronchial vascular system which, by virtue of the expansion of that portion of the bronchial venous bed flowing into the azygos system, may have had a safety valve to cope with the conditions of Dr. Burke's experiments.

DR. OSLER ABBOTT, Atlanta.—I wonder if I might be permitted to draw attention to some other experiments which have been carried on in this line by Nature, namely, in the form of disease. The two primary ones I think of are, first, the extremely severe and tight mitral stenosis, in some of which, as you know, it is extremely difficult to see at autopsy how the venous return to the lung got to the left ventricle. Second, is the occasional patient with bronchiectasis in which the resected specimen is characterized by a long-standing and well-recognized thrombosis of the pulmonary vein of the segment or lobe. I think it offers a very important clue, because in those instances there has been observed considerable dilatation and varicose formations of the bronchovenous system. I think another point is that we must stress the susceptibility of such areas of the lung, or any organ with impaired circulation, to infection. This work, then, emphasizes the extreme importance of control of pulmonary suppuration in mitral stenosis. I wonder if I might suggest to Dr. Hanlon the advisability of applying Cellophane prepared by Dr. Hufnagel's technique to the pulmonary venous system, to stimulate Nature's slow progressive experiments.

DR. HANLON.—(Closing.) I would like to thank the discussants for their remarks. With regard to the comments of Dr. Alley, we are cognizant of the anatomy and the anomalies thereof on the left side. Although Dr. Burke did not stress it, the anatomic completeness of the occlusion on the left side was confirmed in all the nonsurviving animals at the time of postmortem examination. As regards the socio-economic factors, I fear I must confess that the social service aspects of our experimental laboratory are rather inadequate at the present time, so that the previous history of these animals is, as he pointed out, unknown to us. With regard to Dr. Abbott's suggestion, I think it is an excellent one. In connection with Dr. H. W. Scott, Jr., Dr. Byron Olson and others, we have been investigating and are continuing an investigation of the effect of congestion brought about by various types of constricting agents on the pulmonary circulation in regard to the therapy of tuberculosis. So far that has been an inconclusive study.

The most important thing to our mind about the present investigation is not the fact that the rate of survival or death can be altered; rather our interest lies in the mechanism by which compensation is brought about. As Dr. Burke mentioned, one would think from the gross and histologic appearance that these lungs might be functional, but it is obvious when one tries to employ such a lung as a ventilatory agent that it is far from adequate functionally.

FURTHER DISCUSSION OF THE RIGHT THORACIC APPROACH TO ESOPHAGEAL LESIONS

R. K. Hollingsworth, M.D., Martinsburg, W. Va.

SINCE it has been demonstrated that the stomach can be brought to any desired height in the thorax, or even into the neck, for esophagogastrostomy, some controversy has arisen over the virtues of the right- versus the left-sided approach. This applies more specifically to lesions of the upper and mid-thoracic esophagus. That lesions in the lower third are best handled through the left side is probably universally admitted. The ready access to the stomach through the left hemidiaphragm, without further external incision, is appealing. But in the higher lesions this advantage must be weighed against the greater difficulty encountered in removing them from behind the aortic arch and from the upper mediastinum. As Lewis[1] has pointed out, on the right, the azygos vein is the only impeding structure, and the aortic arch and the left subclavian artery act as a bolster against the left pleura during dissection. Furthermore, many thoracic lesions involve the azygos and are difficult to handle from the left. Just a few short years ago, before the days of thoracic esophagogastrostomy, the right side was the generally accepted one for the Thorek procedure. But this technically easier operation was overshadowed by the ease with which the stomach can be handled from the left, and this side became the one of choice.

In 1946 Lewis[1] reported a staged procedure in which he first explored the abdomen and mobilized the stomach. At a subsequent operation, the right side of the thorax was explored and, if possible, the esophagus was resected. The previously mobilized stomach was then brought up into the chest through the esophageal hiatus, and esophagogastrostomy was performed. This procedure had two very obvious defects. First, a rather formidable major abdominal operation was performed with no assurance that the second stage would be possible. Second, delay between the first and second stages produced technical difficulties in the form of intra-abdominal adhesions involving the previously mobilized stomach. Kay,[2] in 1941, had encountered this same difficulty. Chamberlain[3] and Pool[4] counter the first objection by performing the anastomosis above the esophageal lesion regardless of whether or not it can be removed. The second objection is obviated by performing the two stages on the same day. Both can be overcome by the use of a right thoraco-abdominal incision which gives a wide, beautiful exposure of the entire area to be attacked. More recently, Harrison and Pickett[5] have described a multiple incision approach, exploring the chest first through the third right anterior interspace, freeing the esophagus and then proceeding to a left abdominal incision to mobilize the stomach. While this has the advantage, as pointed out

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by the authors, of saving time by having two operating teams working simultaneously, one on each incision, it seems to me that technically the removal of the esophagus through an anterior incision could be very difficult.

In this communication, three cases using the right-sided approach are reported. Each presents a different problem from which certain lessons may be learned.

Fig. 1.—Case 1. Preoperative esophagogram.

CASE REPORTS

CASE 1.—S. T., No. 10 579, a 54-year-old white man, was admitted to this hospital on Feb. 24, 1949. He was admitted to the Neurological Service for a nervous disorder. His history indicated that for the past two or three months he had suffered loss of weight and appetite and some epigastric distress following meals. This distress simulated gastric or duodenal ulcer, and in the course of routine barium studies a lesion of the midportion of the esophagus was seen (Fig. 1). On March 11, 1949, an esophagoscopy was done and biopsy made. This revealed a squamous-cell carcinoma. Physical examination and all laboratory studies were within normal limits.

Operation was performed on March 22, 1949. The multiple approach as described by Lewis was done, a left subcostal incision for the abdominal part and through the bed of the resected sixth rib for the thoracic part. The carcinoma had invaded completely through the wall of the esophagus (Fig. 2) and removal was difficult; in fact it was im-

possible to remove all of the growth from the mediastinum, making the procedure entirely a palliative one. The operation was well tolerated, and the patient was returned to his room in good condition. Two months after operation this patient was sent to Walter Reed Hospital where he received deep x-ray therapy, particularly centered over the area where the tumor was known to have been left. At autopsy no evidence could be found that this therapy had been of any benefit.

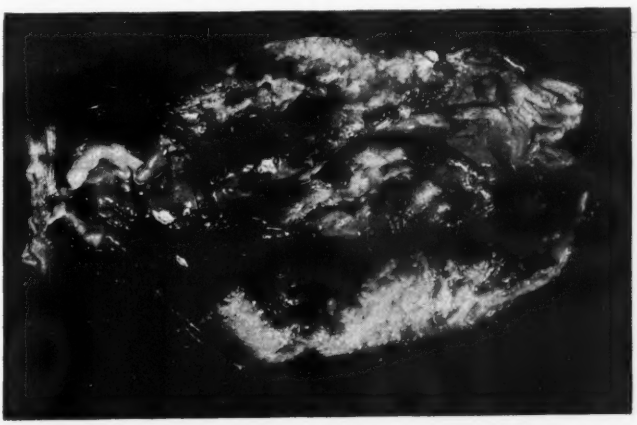


Fig. 2.—Case 1. Surgical specimen. Note invasion of growth through entire wall.

A. *B.*

Fig. 3. (Case 1)—*A*, Portable film immediately postoperative. *B*, Later film showing marked dilatation of stomach with retained food.

Comment.—Immediate postoperative recovery was without incident until the patient began to take food. It was then discovered that while swallowing was normal, the stomach was not emptying, and it became markedly distended. This was thought to be due to a pylorospasm following the vagotomy incident to the resection. This gave considerable difficulty until finally, by the use of a liquid diet, nightly aspirations of the stomach and the use of Doryl, the

stomach recovered sufficient tone to force its contents through the pylorus. Emptying remained slow, and the stomach remained dilated (Fig. 3). However, this did not seem to affect the patient's breathing. Further consideration of this complication led to the belief that perhaps the hiatus was too small. Additional comments on this will be made later.

This man lived seven months, after which he died of extensive metastases. At autopsy there was no evidence of recurrence at the site of the anastomosis. The stomach was markedly dilated and the stoma through the esophageal hiatus admitted two fingers but was filled with thick folds of gastric mucosa.

Fig. 4.—Case 2. Preoperative esophagogram showing stricture.

The site of the original lesion in the mediastinum showed extension of the growth in spite of maximum doses of deep x-ray therapy. Scattered metastatic nodules were seen in the mediastinum, stomach wall, on the right pleura, in the liver, and in the spleen.

Technically, the multiple incision approach was entirely satisfactory in this case, and I feel that mobilization of the esophagus was easier than it would have been from the left side. Throughout the operation the patient's condition was good. It did not appear that the slight increase in time required to open and close the abdomen added to the risk, and mobilization of the

stomach is the same whether done through the abdominal incision or through the left hemidiaphragm. Some time is lost in changing position, re-preparing and draping, and this is a disadvantage.

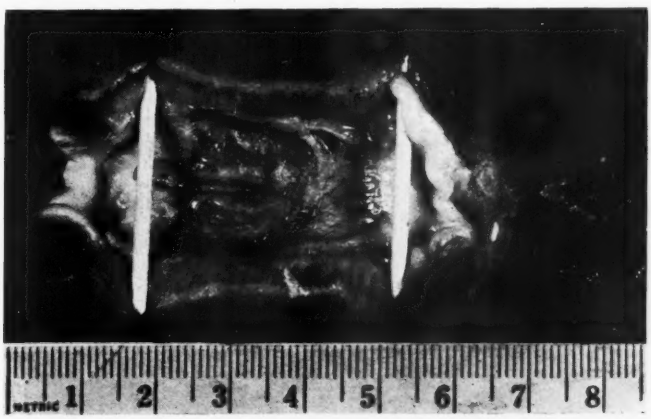


Fig. 5.—Case 2. Surgical specimen showing extent of stricture.

Fig. 6.—Case 2. This shows the level of the anastomosis and the postoperative dilatation of the stomach.

CASE 2.—A. L., No. 8 233, a 49-year-old white man, was admitted to this hospital on Nov. 8, 1948, with the chief complaint of difficulty in swallowing. Three weeks previous to this date he had picked up a bottle which he thought contained whisky, and swallowed its contents. He very promptly determined his error (it was lye) and drank large quantities of milk, chocolate milk, and water, finally vomiting. While remaining on a liquid diet, he continued to vomit daily, usually with the production of some blood. Nine days later he had severe substernal pain, and vomited a large quantity of blood. At the time of his admission here he was unable to swallow anything. Briefly, his treatment from this time until he was referred for surgery on April 25, 1949, consisted of a series of dilations. The stricture could be dilated up to F26, but the relief obtained was of short duration. Physical examination and all laboratory studies were within normal limits.

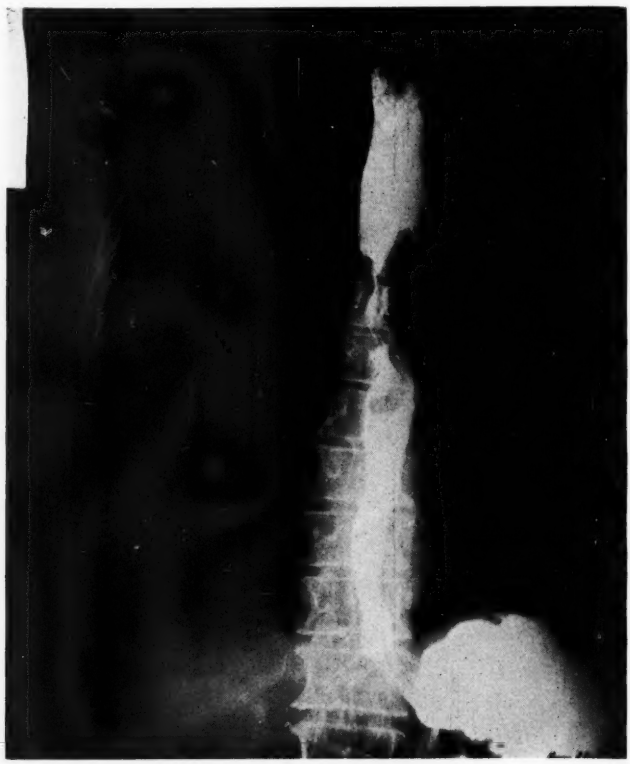
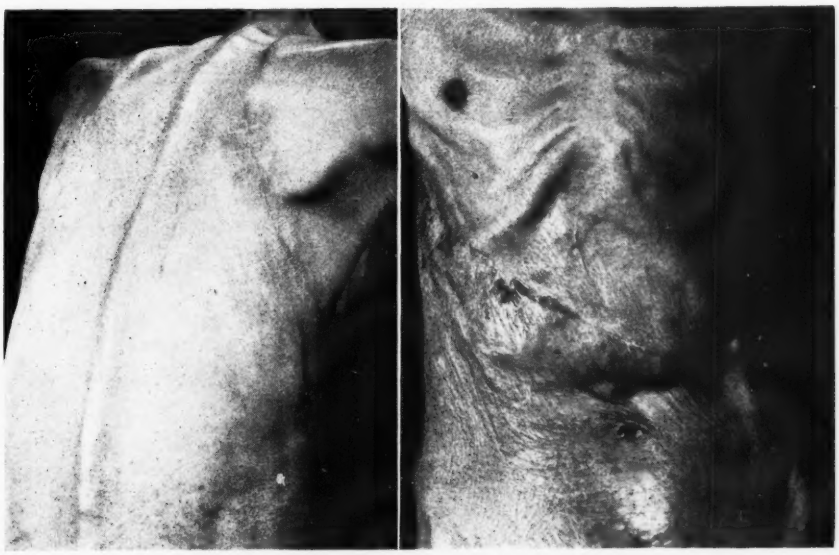


Fig. 7.—Case 3. Preoperative esophagogram.

Operation was performed on May 4, 1949. We were not sure of the exact length of the stricture, but it was hoped that the involved portion could be resected and a direct esophageal anastomosis made. For this reason, a right-sided approach was selected. When the stricture was found to be too long (Fig. 5), complete mobilization of the lower segment of the esophagus, through the hiatus, was done. By drawing up a small amount of the stomach through the hiatus the ends of the esophagus could be approximated. However, it was feared that the blood supply of the lower segment might have been too involved, and when it was found that an adequate amount of stomach could be brought up to reach the upper segment, esophagogastrostomy was felt to be the safest procedure.

The patient withstood the operation well, and made an uneventful recovery up to the time of taking food. As in Case 1, the stomach was slow to empty, but this man had much less trouble even though the stomach has remained dilated (Fig. 6). When seen recently he had no complaints.

Comment.—This case demonstrates the great mobility of the stomach without the division of any of its attachments. The fundus was easily brought up through the hiatus to the right midchest (Fig. 6), and the anastomosis made without undue tension.



A. *B.*

Fig. 8.—Case 3. Showing *A*, thoracic, and *B*, the abdominal portion of the combined thoracoabdominal incision.

Here again the bad effects of the small hiatus crowded with stomach is demonstrated.

CASE 3.—W. F., No. 12 479, a 57-year-old Negro man, was admitted on July 31, 1950, with the chief complaint of difficulty in swallowing. The trouble had begun about two months previously when he said that he felt a "sort of lump in his throat." However, he was able to swallow all right until about three weeks previously when he began to have difficulty with solid foods. The condition progressed rather rapidly from this time, until at the time of admission only liquids could be swallowed. There had been a thirty-pound weight loss in the previous two months, and there had been increasing ease of fatigue.

The past history and family history were noncontributory. His occupation was that of a gardener. Habits were good, smoking being moderate and drinking only a small amount of beer.

The physical examination contributed nothing to the diagnosis. While he was thin and showed evidence of recent weight loss, his general appearance was fair. Temperature and pulse were normal; blood pressure 106/70; weight 137 pounds, usual weight 165 to 170 pounds. All laboratory studies were within normal limits. Roentgenogram (Fig. 7) showed a filling defect in the esophagus extending from about D5 to D9.

At esophagoscopy on Aug. 5, 1950, a fungating mass was encountered at about 25 cm. from the front teeth. A biopsy from this mass was reported as squamous-cell carcinoma.

Operation was performed on Aug. 10, 1950. A right thoraco-abdominal approach was selected. Only such details as are pertinent to this approach will be described. The rest was routine procedure. The patient was placed on his left side, with the body at an angle of about 65 or 70 degrees and the chest and upper abdomen prepared and draped. The incision (Fig. 8) was made along the seventh rib from the spinal muscles posteriorly to the costochondral junction, and the chest cavity entered through the bed of the resected seventh rib. When the esophagus had been mobilized from the thoracic inlet to the hiatus, the rib spreader was removed, the wound covered with sterile towels, and the table rotated toward the right until the abdomen was nearly level. The thoracic portion of the

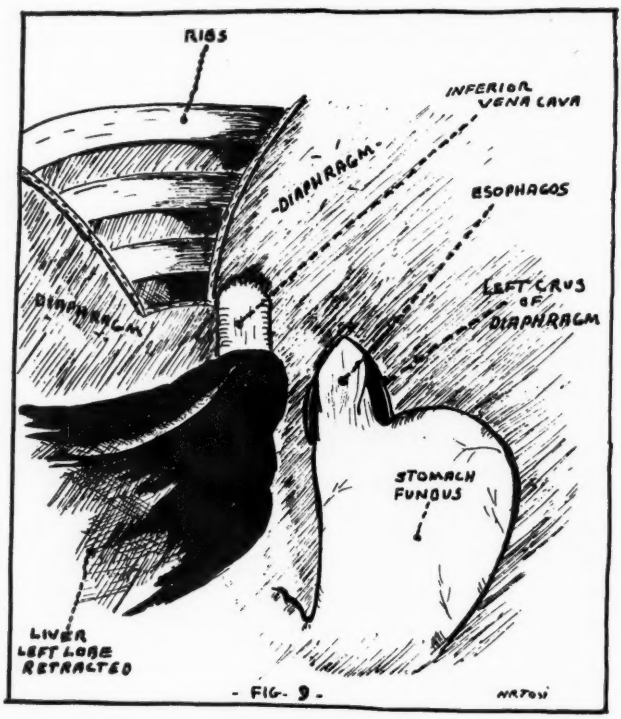


Fig. 9.—Normal relationship between esophagus and inferior vena cava.

incision was then continued across the costal margin to the left side of the abdomen. The hepatic ligament was then divided, mobilizing the left lobe of the liver which was retracted to the right, exposing the entire stomach. The spleen was somewhat enlarged and adherent to the greater curvature of the stomach. It was friable and, while being freed, it was torn and removed. The mobilization of the stomach was routine. With the left lobe of the liver retracted to the right, the entire gastrohepatic ligament was exposed and accessible. On drawing the stomach up into the chest, the cause of the difficulty in emptying the stomach encountered in Case 1, and to a less extent in Case 2, was well demonstrated. The esophageal hiatus is behind and slightly to the left of the inferior vena cava. The size of this hiatus is of relative unimportance. That it will vary in size has been

demonstrated by Harrington.[6] Furthermore, if a larger hiatus is needed the right crus can be divided, giving more room in a transverse direction (Fig. 9). The esophagus in its passage through the lower posterior mediastinum remains to the left of the inferior vena cava. But, to bring the stomach into the right chest, it (the stomach) must pass between the vena cava and the body of the vertebrae (Fig. 10). Palpating through the esophageal hiatus from below one is impressed by the narrow space which exists between the vein and the vertebrae. That there can be serious interference with the emptying of the stomach is quite evident, particularly in view of the loss of tone occasioned by the division of both vagus nerves. The degree of obstruction, other than that caused by section of the vagi, depends on three factors. One, the size of the stomach; two, the thickness of the stomach wall; and three, the size of this space which may vary somewhat indi-

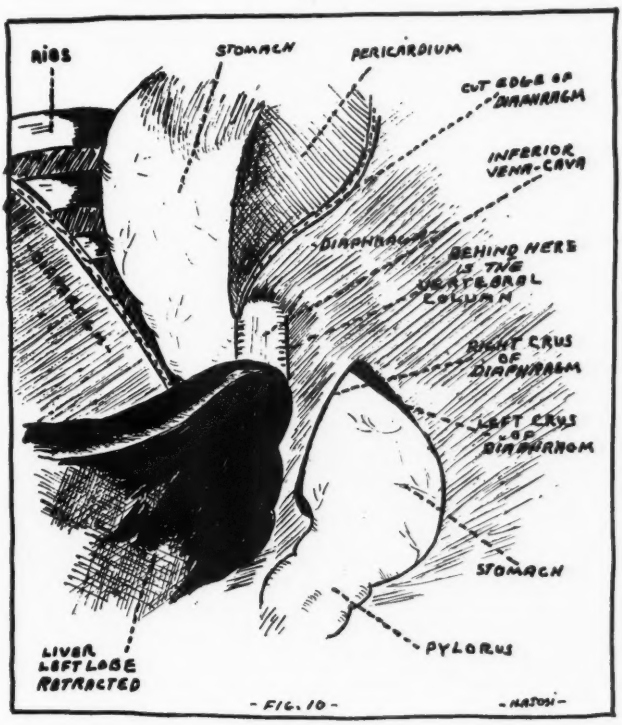


Fig. 10.—Stomach must pass between inferior vena cava and body of vertebrae to reach right chest.

vidually as do all anatomical structures and spaces. The remedy was quite evident: the transplantation of the stomach into the chest anterior to the inferior vena cava. The diaphragm was therefore split down to the vena cava. The esophagus was divided at the cardia and the stump inverted into the stomach. The normal esophageal hiatus was then closed with two interrupted sutures. The stomach could now be brought up into the chest just anterior to the vena cava and the diaphragm sutured to its wall, forming a new adequate hiatus. In addition to relieving the obstruction possibility, this maneuver added several centimeters to the length of the stomach available for high thoracic or cervical anastomosis. Closure of the abdomen, the performing of the anastomosis, and closure of

the chest were routine. The patient withstood the procedure well, and made a good postoperative recovery. Sips of water were allowed on the second day, and soft food was easily swallowed by the end of the first week. There has been no difficulty with emptying of the stomach (Fig. 11). This patient is not believed to be cured, as the mediastinum at about the level of the azygos vein was found to be infiltrated with the cancer, and it is very doubtful that it was all removed. But he is able to eat and has been comfortable these five months since the operation.

Fig. 11.—Case 3. Three months postoperatively. Note tubelike character of stomach.

Comment.—The combined thoraco-abdominal approach was found to be a very satisfactory method of attacking a high or midthoracic esophageal lesion. Because of the mediastinal involvement, I am convinced that esophageal removal was decidedly easier than it would have been from the left side. Exposure of the entire upper abdomen is excellent, and the stomach is easily mobilized from the hiatus to the pylorus.

In spite of the technically easier mobilization of the esophagus from the right side, I must admit that delayed emptying of the stomach encountered in Cases 1 and 2 had left me somewhat discouraged. With the combined ap-

proach, the cause of the difficulty was recognized and easily remedied. Fig. 11 shows the present condition of the stomach. There is no dilation; in fact, it has now assumed a tubelike character.

It must be conceded that this operation is of greater magnitude than the left thoracic approach, with entrance to the abdomen through the diaphragm. However, I believe that in mid or high thoracic lesions the greater ease of mobilization of both the esophagus and the stomach compensates for the more extensive incision. Admittedly, one case is scarcely sufficient properly to evaluate a procedure, but it is enough to demonstrate and evaluate its technical aspects.

SUMMARY

The approach to lesions of the esophagus through the right chest is briefly discussed.

Three cases are reported, each presenting a different problem and from which certain lessons may be learned.

In two cases the bad effects of bringing the stomach through a small hiatus is demonstrated.

In one the great mobility of the stomach without dividing its attachments is demonstrated.

One case is reported, using a right combined thoraco-abdominal incision. If the right approach is to be used, it is believed that this is the most satisfactory incision.

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Announcement

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The 33rd annual meeting of the American Association for Thoracic Surgery will be held March 27, 28, and 30, 1953, in San Francisco, Calif. Headquarters will be at the Hotel Fairmont. Suitable accommodations also have been reserved at near-by hotels, the Mark Hopkins, the Huntington and the Sir Francis Drake.

Requests for Hotel Reservations

These should be mailed to Dr. H. Brodie Stephens, Chairman of Hotel Committee, American Association for Thoracic Surgery, Room 200, 61 Grove St., San Francisco 2, Calif. The following information must be included: (1) two choices of hotels; (2) type of accommodation desired—single, double, twin, room or suite; (3) name of other room occupants, if any, whether wife or another doctor; (4) date and approximate hour of arrival; (5) date of departure; (6) return address.

Abstracts for Papers

Abstracts for the presentation of papers at the 1953 meeting must be received on or before Dec. 1, 1952, otherwise they will not be considered by the Program Committee. *Five, repeat, five* copies of each abstract should be sent to the Secretary of the Association, Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif. They should not be sent to the Editor.

The abstracts should contain from 200 to 250 words, and should accurately reflect the contents of the completed paper.

Applications for Membership

Completed membership applications must reach Dr. Edward M. Kent, Chairman of the Membership Committee, 1107 Clark Bldg., Pittsburgh 22, Pa., on or before Dec. 1, 1952, in order to be acted upon at the annual meeting in San Francisco.

All correspondence regarding membership, including requests for membership applications, should be addressed to Dr. Kent.